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Non-infarctual ST elevation and acute cardiopulmonary failure in carbon monoxide poisoning: a case report

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Abstract. – OBJECTIVE: Carbon monoxide is produced by the incomplete combustion of organic fuel. In the United States, it is responsible for about 500 deaths annually. Increased carboxyhemoglobin concentration and hypoxia disrupt cardiac myocyte integrity and cause dysrhythmias, acute cardiac failure and coronary artery disease. We described a case of a patient with CO-poisoning and ST elevation at ECG precordial leads who developed severe transient heart failure.

CASE PRESENTATION: A 57-year-old man was admitted to the emergency department for acute carbon monoxide poisoning that led to respiratory and cardiac failure. The electrocardiogram showed ST elevation in precordial leads, but the coronary angiography was normal. The patient was successfully treated and discharged. Three days later he was readmitted for similar symptoms and subsequently died. We hypothesize that the ECG findings were related to transient coronary vasospasm due to CO poisoning and that acute respiratory and cardiac failure related to carbon monoxide toxicity caused death.

CONCLUSIONS: The management of patients poisoned by carbon monoxide requires early identification and intensive treatment and a careful evaluation of the home environment prior to discharge. ST elevation in such patients may be related to coronary vasospasm.

Key Words:
Carbon monoxide, Cardiac failure, Coronary vasospasm, STEMI.

Abbreviations

Carbon monoxide (CO), ST elevated myocardial infarction (STEMI), not ST elevated myocardial infarction (NSTEMI), Central Nervous System (CNS), oxygen (O2), Delayed Neurological Sequelae (DNS), carboxyhemoglobin (COHb), The Italian Society of Emergency Medicine-Urgency (SIMEU), The Italian Society of Underwater and Hyperbaric Medicine (SIMSI), hemoglobin (Hb), peripheral oxygen blood saturation (SpO2), electrocardiogram (ECG), intensive care unit (ICU), Acute Heart Failure (AHF), transthoracic echocardiogram (TTE), Acute Heart Failure (AHF), European Society of Cardiology (ESC), creatine kinase (CK), creatine kinase-muscle/brain (CK-MB), amino-terminal fragment of pro-brain natriuretic peptide (NT-proBNP), Emergency Room (ER), pulseless electric activity (PEA), acute respiratory failure (ARF), ejection fraction (EF).

Introduction

Acute carbon monoxide (CO) intoxication is the most common type of accidental poisoning in industrialized countries and is responsible for 40-50,000 emergency department visits in the United States[1,2]. CO is a colorless, odorless, tasteless, and non-irritating gas produced by the incomplete combustion of any type of organic fuel in conditions of oxygen deficiency[3-8]. Small amounts of CO are physiologically produced by enzymatic reactions, the most important of which is catalyzed by heme oxygenase (HO)[9,10]. Its toxic effects include inflammation, interruption of cellular respiration, oxidative stress, and apoptosis with the activation of hypoxia-inducible 1α factor (HIF-1α) and neurologic and cardiac damage[11]. The main signs and symptoms mimic a gastrointestinal infectious disease and include headache, dizziness, nausea, and vomiting[12,14]. Among its acute neurological manifestations, we find con-

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fusion, concentration deficit, initial irritability followed by lethargy and coma[14]. The delayed manifestations, also known as Delayed Neurological Sequelae (DNS), are seen in about 30% of cases and can sometimes occur a long time after exposure[15-18]. The cardiac manifestations assume great clinical significance since the cardiocytes are highly sensitive to hypoxia and ischemia caused by the disruption of mitochondrial oxidative reactions by elevated CO levels[19]. Since CO intoxication frequently presents with non-specific signs and symptoms, it may not be diagnosed rapidly[20] and is frequently confused with other acute diseases[21,22]. In most of the cases, the determination of the plasma levels of carboxyhemoglobin (COHb) confirms the diagnosis[23]. Plasma levels of COHb are not predictive of the severity of intoxication unless levels are 40-50% higher than the baseline[24]. This depends on time elapsed between exposure and subsequent determination of plasma COHb and on the ability of the lungs and kidneys to eliminate carbon monoxide from the organism[25,26]. The Italian Society of Emergency Medicine-Urgency (SIMEU) has proposed a severity grading based on clinical manifestations[27].

CO cardiotoxicity is well documented. CO-induced cardiac toxicity was reported for the first time in 1865, when Klebs et al[28] described diffused hemorrhagic spots in the cardiac tissue. CO is cardiotoxic and the damage can be reversible or permanent[29-31]. CO toxicity derives from the combination of tissue hypoxia and direct CO-mediated cellular damage[32]. It competes with molecular oxygen (O_2) for hemoglobin (Hb) binding sites, with an affinity 200-250 times higher than O_2. The binding of Hb with CO forms COHb, which reduces the hemoglobin available for oxygen transport to the tissues[33]. Moreover, the release of O_2 to the tissues is altered because of COHb shifts the oxyhemoglobin dissociation curve to the left, making its shape more hyperbolic[34]. Free dissolved CO damages the heart directly: it competes O_2 for cytochrome-a[35,36] and inhibits cardiac cytochrome-oxidase activity interfering with mitochondrial cell respiration[37]; it also binds intracardiac myoglobin heme, by inhibiting myoglobin-dependent O_2 uptake[38]. An additional element of cardiotoxicity of CO results from the oxidative stress: the overproduction of oxygen free radicals overwhelms antioxidant defensive capacity, resulting in cell damage[15]. These observations support the hypothesis that CO poisoning causes a stunned myocardial syndrome[39]. This syndrome consists of transient and reversible ventricular dysfunction, which occurs when reperfusion follows a short ischemic event[40]. The cardiac damage most commonly displays with tachycardia[41], dysrhythmias and electrocardiographic alterations[42], myocardial infarction[43,44], pulmonary edema, and cardiogenic shock[45]. The electrocardiographic changes are not correlated to COHb concentration[46]. The CO can unmask an unknown coronary arterial disease leading to a myocardial ischemia[33]. Myocardial ischemia and necrosis have been described even in patients with healthy coronary arteries[43]. Therefore, when CO intoxication is suspected, coronary angiography should be considered in order to rule out undiagnosed coronary artery disease[47]. A few cases of ST elevation without significant coronary stenosis has been described and related to coronary spasm and variant angina[48,49].

Case Report

A 57-year-old Caucasian man was admitted to the Emergency Department due to anxiety, confusion, tachycardia, and dyspnea. The patient did not report any significant past medical history. The patient did not take any medication, did not consume alcohol, and did not smoke. Admission vital signs were noted: regular radial pulse with an average heart rate of 110 beats per minute, arterial pressure of 180/90 mmHg and peripheral oxygen blood saturation (SpO_2) of 90% in ambient air and spontaneous breathing with an average respiratory rate of 25 breaths per minute. The axillary temperature was normal. Cardiac examination revealed a regular rate and rhythm with normal heart sounds and a holosystolic murmur at the apex. Chest examination noted symmetrical thoracic activity, normal expansion, and bilateral basal end-inspiratory crackles. Abdominal examination was normal; no swelling of the feet or legs was detected but the extremities were cold. The patient was alert, answered simple questions accurately and was able to execute simple tasks; the pupils were equal, round and normally reactive to light; the neurological examination was normal. The patient lived in the countryside and used a pellet stove to heat his bedroom without any aeration system. An arterial blood gas analysis showed respiratory acidosis with hyperlactatemia, increased anion gap, and a concentration of COHb above 15%. CXR detected pulmonary edema. The ECG showed sinus tachycardia with ST-segment elevation in the precordial V1-V6 leads.

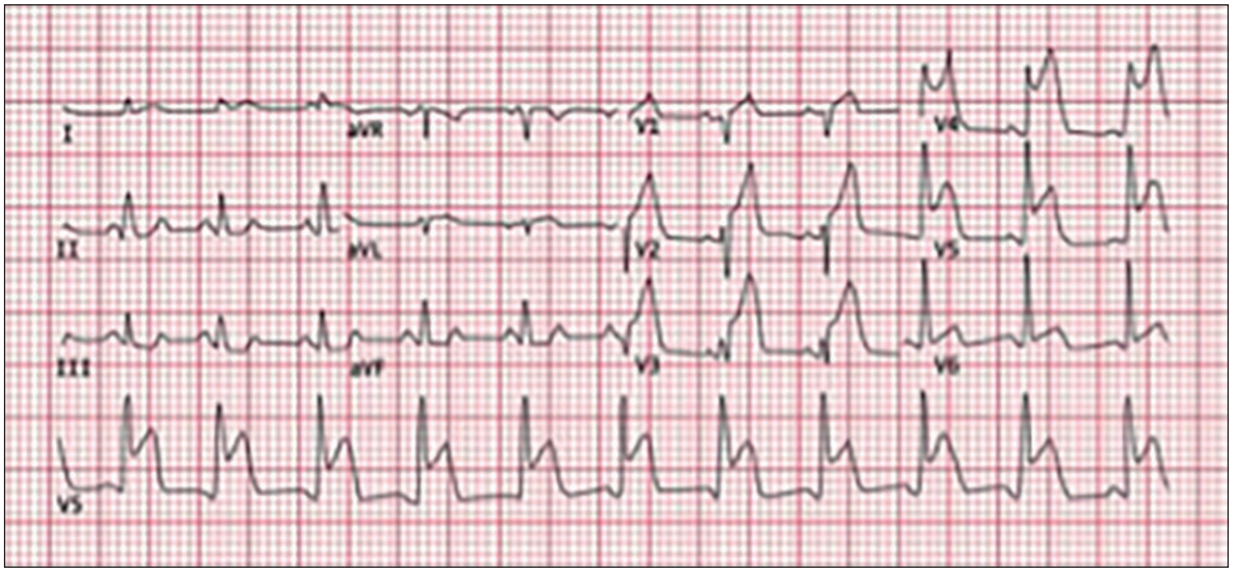

Figure 1. ST-elevation is correlated with myocardial infarction, pericarditis, and myocarditis. Probably the acute myocarditis that occurred in this patient is due to chemical damage of CO on myositis or to vasospasm.

The patient rapidly decompensated with the onset of hypotension (systolic BP < 90 mmHg), worsening hypoxemia, and respiratory acidosis. He was admitted to the Intensive Care Unit (ICU). Acute Heart Failure (AHF) with cardiogenic shock and respiratory failure was suspect-

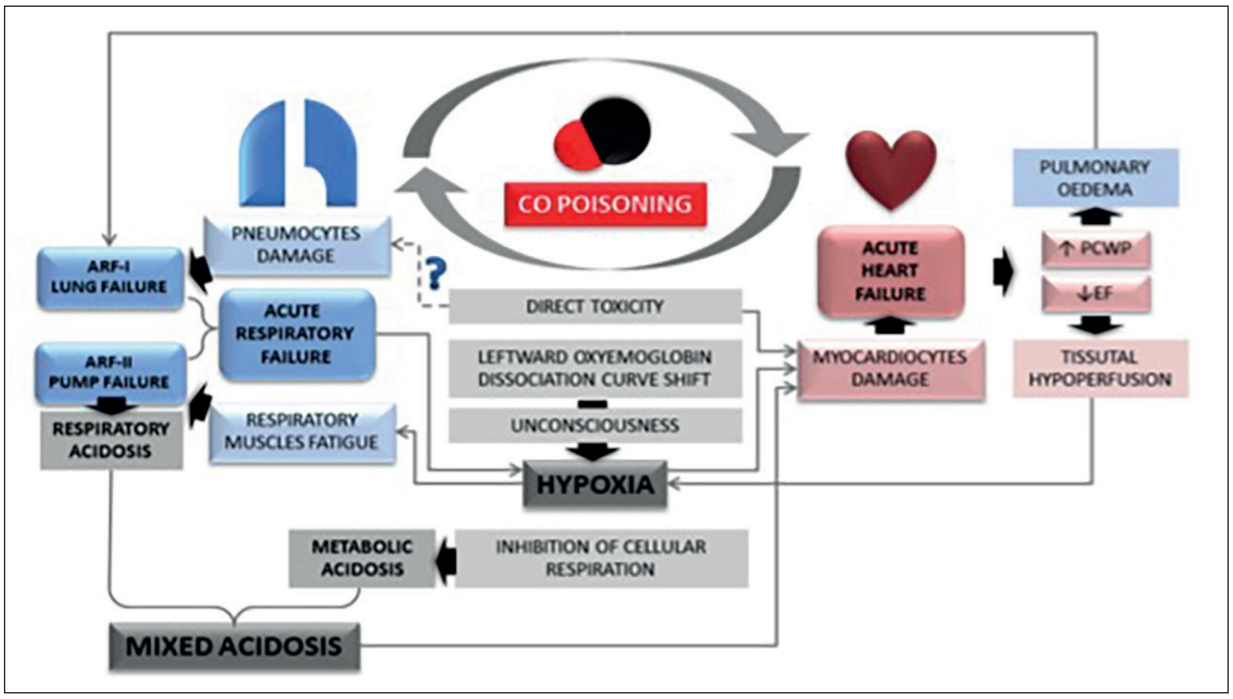

Figure 2. Mutual effects of the CO poisoning on the cardiac and pulmonary function. The carbon monoxide (CO) displays direct toxicity on the myocardiocytes leading to acute heart failure (AHF) and thus to pulmonary edema and to acute respiratory failure (ARF) type I (lung failure). Little is known about a direct effect of this toxic gas on the pneumocytes. The CO is also responsible for indirect effects by establishing a hypoxic condition that is multifactorial (leftward shift of the oxyhemoglobin dissociation curve, unconsciousness, tissue hypoperfusion) and a mixed acidosis. The hypoxia exacerbates the AHF by affecting the contractile function of the myocardiocytes and sustains an ARF type II (pump failure) by causing the fatigue of the respiratory muscles.

ed. A transthoracic echocardiogram (TTE) was performed and demonstrated globally reduced left ventricular contractile function with ejection fraction of 20-25% and a severe mitral regurgitation; the pericardium was normal. The patient was treated with ventilatory and circulatory support. He underwent an orotracheal intubation under sedation with subsequent lung protective mechanical ventilation and inotropic support. The patient responded quickly, and peripheral perfusion was restored. As the patient was confused and had cardiovascular failure and acidosis, hyperbaric oxygen therapy was started and maintained until COHb concentration was reduced to normal values (<3%)[25,50]. Blood cell count, electrolytes, renal, liver, and thyroid function were all within the normal range. Creatine kinase (CK), creatine kinase-muscle/brain (CK-MB), troponin and lactate dehydrogenase (LDH) were higher than the normal value. The amino-terminal fragment of pro-brain natriuretic peptide (NT-proBNP) was slightly elevated. The ECG showed a pattern indicating an Acute Coronary Syndrome (ACS). Given the ECG findings and the increased concentration of myocardial necrosis markers, a coronary angiography was performed but it did not detect any stenosis or other abnormalities of the coronary arteries. It was supposed that ECG finding was related to coronary vasospasm related to CO intoxication. After 12 hours of mechanical support, lung function improved, and no further evidence of cardiopulmonary failure was observed. The subsequent arterial blood gas analysis was normal, and the radiogram of the chest showed no further evidence of pulmonary edema. The cardiac necrosis markers decreased to normal levels. The TTE was repeated and detected an improved EF to 50-60% with no global dysfunction; mitral regurgitation was no longer documented. The patient was extubated and discharged to the Internal Medicine (IM) ward for monitoring and care. He remained hemodynamically stable for the following two days and discharged. Three days later, he was re-admitted to the Emergency Room (ER) with the same cardiovascular condition. He had the same TTE pattern of the previous admission with decreased ejection fraction (EF) and global left ventricular dysfunction. The measured COHb level was higher than 20%. He died from acute cardiac failure and cardiac arrest with pulseless electric activity (PEA) despite prompt treatment and resuscitative measures.

Discussion

As described in the literature and confirmed by our clinical case, blood COHb concentration is not a reliable prognostic marker in the CO-poisoned patient. In this case, the patient outcome was deadly, despite the normalization of COHb concentration after the hyperbaric oxygen therapy and the initial recovery. This can be explained by the accumulation of large amounts of CO in the tissues and its subsequent release, which can lead to coma and fulminant cardiorespiratory failure[51]. In addition to the toxic mechanisms described so far, we hypothesize that acute heart failure and acute respiratory failure induced by CO worsen one another. We can reasonably state that the initial impairment in both lung and heart function is sustained by hypoxia which depends on two main factors: the leftward shift of the oxyhemoglobin dissociation curve and the interruption of cellular respiration due to inhibition of the mitochondrial IV complex[17]. In addition, CO-poisoned patients may be unconscious this leading to impaired ventilation and thus to acute respiratory failure (ARF) type II (pump failure). Pump failure causes carbon dioxide (CO_2) retention with respiratory acidosis; at the same time, the interruption of cellular respiration due to inhibition of the mitochondrial IV complex causes metabolic acidosis[52]. The hypoxia and the acidosis are responsible for myocardial damage and subsequent reduced EF heart failure with high capillary wedge pressure (PCWP). The increase of PCWP explains the onset of pulmonary edema which itself sustains a type I acute respiratory failure (ARF-I) also known as lung failure. The ARF-I maintains the hypoxia that causes the fatigue of respiratory muscles that is itself a cause of ARF-II. Moreover, severe acidosis is known to increase the effects of parasympathetic nervous activity. It is possibly due to interfering with the hydrolysis of acetylcholine by acetylcholinesterase that will result in a depression of the respiration[12]. While the CO direct toxicity on the cardiac and nervous cells is well described in the literature[32-34], little is known about a possible direct damage on the pneumocytes. Reilly et al[53] have investigated the role of air pollution on lungs and have concluded that long-term low-to-moderate air pollutants exposure is associated with an increased risk of Acute Respiratory Distress Syndrome after severe trauma. Althaus et al[54] have studied the effects of CO on the alveolo-capillary

barrier and have detected a perturbation of the transepithelial ion transport and alveolar fluid reabsorption by the inhibition of epithelial sodium channels.

Conclusions

CO poisoning remains a current issue in Emergency Medicine and it must be suspected when a patient presents with non-specific symptoms that mimic a gastrointestinal syndrome, with or without neurological involvement. Environmental factors should be accurately considered when collecting the medical history of the patient. If CO poisoning is suspected, the patient must be treated in an ICU in order to support his vital functions with special regard to cardiac and pulmonary function. Since CO is known to be cardiotoxic, any cardiac involvement must be ruled out by exploring the electrical, mechanical and histological integrity of the cardiac muscle. For this reason, ECG, echocardiogram, and determination of cardiac necrosis biomarkers must be performed. In the case of cardiac involvement, a coronary catheterization and subsequent angiography should be performed to identify any structural abnormality of cardiac circulation as CO can also unmask a coronary artery disease. The cardiac manifestations of CO poisoning can be reversible or permanent and can include AHF. Besides cardiac dysfunction, a CO-poisoned patient can manifest a mixed ARF, which is sustained by both a lung (type I) and a pump (type II) impairment. AHF and ARF are both triggered by the CO-induced hypoxia but it is possible to identify further, more complicated and interrelated mechanism that may be interrupted by early and aggressive therapeutic intervention which include hyperbaric therapy, hemodynamic and ventilatory support. Deleterious effects of CO poisoning can reappear after a remission period suggesting that the CO accumulated in the tissues can maintain its toxic effects. All this data suggest that, although the study of the CO pathophysiology started at the end of the 19th century, many of the effects of this gas on the human body are still unclear and should be investigated in order to identify a new and better target for the CO intoxication treatment.

Conflict of Interest

The Authors declare that they have no conflict of interests.

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