Troponin elevation reflects myocardial injury in carbon monoxide poisoning

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ABSTRACT

We describe the case of a 48-year-old white man, who was admitted to the emergency department with neurologic deficits and high suspicion of carbon monoxide (CO) poisoning. Blood carboxyhemoglobin (COHb) level was found substantially increased (i.e., 18%). Clinical symptoms of myocardial infarction were lacking and the medical history was negative for major risk factors of coronary heart disease. However, electrocardiogram and troponin value were both suggestive for an acute coronary syndrome (i.e., a highly-sensitive troponin T value of 0.12 μg/L), while the echocardiogram showed hypokinesia of left ventricular apical lateral wall. The coronary angiogram performed one week after admission did not reveal the presence of coronary obstructions. It is hence assumed that high levels of COHb in blood, such as after CO exposure, may trigger myocardial injury by severe generalized tissue hypoxia (i.e., impaired oxygen delivery) and a direct toxic effect on myocardium. Contributing factors that also decrease myocardial oxygenation include inadequate myocardial perfusion and prothrombotic state. This case report suggests that increased troponin values, especially when measured with highly-sensitive immunoassays, may be observed in patients with CO poisoning, and mirror the presence of myocardial injury. Therefore, although the measurement of cardiac biomarkers may be advisable in the presence of CO toxicity to identify cardiac involvement, caution should be used when troubleshooting the underlying source of troponin elevations in order to preven t overdiagnosis or misdiagnosis of acute coronary syndrome.

INTRODUCTION

Cardiac troponins represent the recommended biomarkers for the detection of myocardial injury, risk stratification in patients suspected of acute coronary syndrome (ACS) and for the diagnosis of myocardial infarction (MI) (1). In the last years, technological advances have led to the development of troponin immunoassays with remarkable improvements in analytical sensitivity (i.e., lower limit of detection). Apple et al. have suggested that the term “highly-sensitive” (HS) be reserved to those assays with total imprecision (CV) ≤10% at the 99th percentile upper reference limit and which allow to obtain measurable concentrations in at least 50% (ideally 95%) of healthy individuals (2). HS-assays display an excellent diagnostic performance for the workup of patients with chest pain at the time of their initial presentation (3). However, as a consequence of the improvement of the clinical sensitivity, the number of false positive results for patients suspected of acute MI is increased (4). Accordingly, several non-MI patients with cardiac injury (i.e., myocarditis, sepsis, heart and renal failure, cardiotoxic drugs, poisoning) can produce troponin results that mimic acute MI. Therefore, serial troponin testing must be used in conjunction with anamnestic and clinical presentation, by including signs and symptoms, electrocardiographic (ECG) findings and imaging results (5).

CASE REPORT

A non-smoker 48 years old male was found very confused in an utility enclosed room located in the basement and equipped with a old propane-gas boiler. He was urgently admitted to the emergency department (ED) with headache, malaise, fatigue, nausea and

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dizziness. Neurologic examination showed a decreased cognitive ability, disorientation and visual disturbances. On physical exam, vital signs were within physiological limits and no particular physical findings were found. The body temperature was 36.3 °C, systolic and diastolic arterial blood pressure was 110/60 mmHg, pulse was 120 beats per min (bpm) and respiratory rate was 15 breaths per min. The patient's common biochemical tests were within their reference intervals including oxygen saturation (SpO2) obtained from pulse oximetry (96%), except for troponin T (TnT) measured with a HS assay (Roche Diagnostics) (Table 1).

At admission, clinical symptoms of myocardial injury were absent and the medical history was negative for cardiovascular risk factors, including diabetes mellitus, smoking, hypertension or dyslipidemia. The chest was clear to auscultation and physiological heart sounds without murmur were present. ECG findings were, however, suggestive for myocardial injury, including poor R wave progression with terminally symmetric T waves in leads V1 through V6. The increased concentration of TnT (120 ng/L) was also consistent with non-ST-elevation MI. The echocardiographic examination showed left ventricular global hypokinesia, which improved steadily after oxygen treatment.

Anamnestic medical records related to exposition of a potential source of carbon monoxide (CO) and symptoms consistent with CO poisoning were highly indicative for the emergency physician to put forward the clinical diagnosis of CO poisoning. To confirm the clinical suspicion, venous blood carboxyhemoglobin (COHb) level was assessed, yielding a value of 18%. A 100% oxygen treatment through non-rebreather mask was then promptly started and neurological signs regressed quickly and patient becomes more alert.

The coronary angiogram performed one week after admission failed to show evidence of coronary obstructive lesions or a significant burden atherosclerotic disease. The patient was then discharged in good clinical condition.

Table 1
Results of laboratory tests at admission of the patient to the emergency department

Test	Result (reference interval)
Hematology	
Hematocrit, %	46.5 (38.0-49.0)
Hemoglobin, g/L	152 (130-170)
Red blood cells (10^{12}/L)	4.05 (4.20-5.70)
White blood cells (10^9/L)	7.88 (4.30-10.0)
Platelets (10^9/L)	261 (150-400)
Coagulation	
Fibrinogen (g/L)	2.1 (1.5-4.0)
PT (ratio)	0.97 (0.80-1.14)
PT (INR)	0.98 (0.81-1.13)
APTT (ratio)	0.85 (0.85-1.17)
Biochemistry	
P-Creatinine (μmol/L)	76.8 (53.0-114.9)
P-Sodium (mmol/L)	139 (135-145)
P-Potassium (mmol/L)	3.8 (3.4-4.7)
P-Chloride (mmol/L)	99 (98-107)
P-Glucose (mmol/L)	5.6 (3.3-5.6)
P-Troponin T (ng/L)	120 (<14)

PT, prothrombin time; INR, international normalized ratio; APTT, activated partial thromboplastin time.

DISCUSSION

CO is a colorless, odorless, tasteless and non-irritant toxic gas. The leading CO sources include both natural and man-made, and may be present either at home or in the workplace. In particular, CO is formed as a consequence of improper or incomplete burning of natural gas or carbon-based fuels such as propane, gasoline and kerosene. Other causes of CO generation include unvented or improperly vented heaters and furnaces, gas appliances or heaters in small and enclosed spaces, and faulty central heating systems. This compound can also be found in high concentration in tobacco smoke and in the exhaust gas of not catalyzed vehicles.

Acute CO intoxication is the most common framework of accidental poisoning in industrialized countries (6), typically during winter months. Inhaled CO is mainly eliminated by the lungs as an unchanged gas, <1% is oxidized to carbon dioxide and 10%-15% is bound to proteins, especially hemoglobin, myoglobin and cytochrome c oxidase. Immediately after inhalation, the compound diffuses easily into the blood of pulmonary capillaries, crossing the alveolo-capillary membrane. The half-life of CO in breathing room air is nearly 4-5 h, but decreases to approximately 90 min while breathing high-flow oxygen via a non-rebreathing mask (7).

The leading pathophysiological mechanism supporting CO toxicity resides in the ability to bind with high affinity to hemoglobin molecules (6); wherein CO is characterized by 230 to 270-time more affinity than oxygen for human hemoglobin. The leading consequences of this phenomenon are that the toxic compound combines with the heme group, displaces oxygen and finally produces COHb. The newly generated COHb then induces a left shift of the oxygen-hemoglobin dissociation curve, thus lowering the arterial oxygen partial pressure (PaO_2) and impairing oxygen release to peripheral tissues. Additional mechanisms are involved in CO-induced pathology, including direct cellular changes involving immunological or inflammatory mechanisms, inhibition of the electron transport chain through the binding of CO to cytochrome oxidase a, production of oxygen radicals resulting from the conversion of xanthine dehydrogenase to xanthine oxidase, ATP depletion, lipid peroxygenation, apoptosis and reoxygenation injury (8).

The clinical manifestation typically involves organs

with high oxygen demand, very sensitive to hypoxia, especially the central nervous and cardiovascular systems. Moderate to severe CO poisoning is a frequent cause of myocardial injury, both in healthy subjects and in patients affected by atherosclerotic disease (9, 10). The pathogenesis of myocardial damage during CO intoxication is multifaceted and the spectrum of injury is large and often independent from COHb levels, including ACS, cardiac dysfunction, ischemia, infarction, fibrosis, atrial thrombus, arrhythmias and cardiac arrest (9, 11). Accordingly, ECG findings are extremely heterogeneous, ranging from sinus tachycardia to QT prolongation as well as P wave elevation, atrial fibrillation, T-wave inversion or ST depression (12). Conversely, ST-segment elevation is a rare presentation in CO poisoning (13). In a study performed on 230 CO-poisoning patients, only 4% of subjects displayed ST-segment abnormalities, whereas 26% had ST- or T-wave changes (14).

As previously anticipated, COHb may trigger myocardial damage by generalized tissue hypoxia (resulting from a sudden imbalance between myocardial demand for oxygen and supply), as well as from direct toxic effect on myocardial mitochondria. Contributing factors that might also decrease myocardial oxygenation include inadequate myocardial perfusion and increased thrombotic tendency. Moreover, CO causes platelet-neutrophil aggregation and neutrophil degranulation, thus triggering the release of myeloperoxidase, proteases and reactive oxygen species, which cause oxidative stress, lipid peroxidation and apoptosis.

The diagnosis of CO poisoning is mainly clinical and is further supported by the evidence of increased levels of COHb in blood (15). Despite several efforts in the past decades, the search for other specific biomarkers of CO poisoning and toxicity has remained elusive. In particular, controversial results were published on the use of inflammation biomarkers such as C-reactive protein, fibrinogen, chemo-cytokines, interleukins and metalloproteinases for gathering useful prognostic information (16). Moreover, most of these markers are unavailable in clinical practice, due to cumbersome techniques that are mostly unsuitable for large volume of samples and fast turnaround time. As such, COHb remains the only established marker for the diagnosis and monitoring of CO-poisoning (17). Since most standard pulse oximeters are unable to differentiate between the standard oxyhemoglobin molecule and the toxic COHb compound, thus resulting in apparently normal SpO2 (18), in the suspect of CO poisoning it is highly recommended to use a co-oximeter (19), a device that spectrophotometrically reads the percentage of the total hemoglobin saturated with CO (20).

Cardiac biomarkers, namely cardiospecific troponins, are indeed useful for diagnosing and monitoring myocardial injury. An increase of cardiac markers has been observed in 35% to 37% of patients having cardiac manifestations (14). It is hence predictable that the progressive introduction in clinical and laboratory practice of HS troponin immunoassays, which are characterized by remarkably improved analytical sensitivity (21), may represent a breakthrough for assessing cardiac injury in patients with CO poisoning. These methods, including that used in this report, allow to identify mild to moderate myocardial injury in a wide spectrum of non-ischemic cardiac disorders (22), and also offer meaningful prognostic information since patients with increased values on ED admission have an increased risk of total and cardiovascular mortality, regardless of the underlying cause of troponin elevation (23).

In conclusion, the description of this case suggests that increased troponin values may be observed in patients with CO poisoning, especially when measured with HS immunoassays, and reflect the presence of myocardial injury. Although the measurement of sensitive cardiac biomarkers may hence be advisable in patients admitted to the ED (24) for identifying cardiac involvement in the presence of CO toxicity, caution should be used when troubleshooting the underlying source of troponin elevations in order to prevent overdiagnosis or misdiagnosis of ACS (25).

CONFLICTS OF INTEREST

No authors declared any potential conflicts of interest.

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