Case Study

Hydrogen Sulfide Intoxication with Dilated Cardiomyopathy

Hong Seung Lee1, Jun Kwan2, Jong-Han Leem3, Shin-Goo Park1, Eui-Cheol Lee1, Jun Kwang1, Jong-Han Leem3, Shin-Goo Park1

1Department of Occupational and Environmental Medicine, College of Medicine, Inha University, Republic of Korea
2Department of Internal Medicine and 3Department of Occupational and Environmental Medicine, College of Medicine, Inha University, Republic of Korea

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Hydrogen sulfide (H2S) is a colorless, heavier-than-air, inflammable, highly toxic irritant and chemical asphyxiant gas, which has a characteristic rotten-egg odor that is detectable at concentrations as low as 0.5 ppb, but this warning property may be lost in 2 to 15 min at concentrations over 100 ppm through olfactory fatigue. Hydrogen sulfide is generated naturally by decaying sulfur-containing proteins and is released from sewage sludge, liquid manure, sulfur hot springs, and natural gas. It is also a by-product of many industrial processes, including petroleum refining, sewage disposal, mining, wood pulp processing, rayon manufacturing, manure processing, sugar-beet processing, fish processing and hot-asphalt paving. Hydrogen sulfide is especially risky in confined spaces such as fishing-ship holders, manure pits, and sewers. In the United States, 52 deaths related to hydrogen sulfide were reported from 1993 to 1999 in various industries. The toxic mechanism of hydrogen sulfide comprises inactivating cytochrome oxidase in mitochondria and then preventing the cellular metabolism of oxygen. Via this mechanism, hydrogen sulfide can induce hypoxic brain damage and hypoxic cardiac damage as well as mucosal irritation and pulmonary edema. Nevertheless, few cases of cardiac damage following hydrogen sulfide exposure have been reported. We here report a case of dilated cardiomyopathy after hydrogen sulfide inhalation in a sewer worker, the first case report of dilated cardiomyopathy caused by hydrogen sulfide.

Case Presentation

A 24-yr-old male worker at a sewage disposal plant was transferred to the emergency medical center of a university hospital under the impression of myocarditis and acute myocardial infarction. He had suddenly collapsed two minutes after entering a manhole without respiratory protection to rescue an unconscious coworker. He was rescued in seven minutes and transferred to the emergency room of a nearby hospital within 30 min. On arrival, his mental state was confused, and initial vital signs were blood pressure of 125/80 mmHg, heart rate at 120 beat per minute, and respiratory rate at 24 breaths per minute. There were crackles on both lung fields and regular heartbeats without murmur. His arterial blood gas was pH 7.5, pCO2 13.4 mmHg, pO2 133.5 mmHg, and HCO3 15.8 mmol/l. In the complete blood count and chemistry panels, there were no remarkable results except WBC 19,900/mm3 and serum glucose 206 mg/dl. He had had Wolff-Parkinson-White (WPW) syndrome since high school, and this was evident in his electrocardiogram (ECG). Chest radiograph on arrival revealed pulmonary edema on the left lung field. On hospital day 3, liver enzymes were elevated, with aspartate aminotransferase (AST) 162 IU/l, and alanine aminotransferase (ALT) 47 IU/l. Abdominal ultrasound scan revealed findings compatible with toxic hepatitis such as blurred swelling of the liver with increased echo, blurred marginated porta hepatis and biliary tree. AST and ALT peaked to 791 IU/l, 397 IU/l on hospital day 6 and 10 respectively, and then decreased. Pulmonary congestion on chest radiograph was improved but substernal pain on cough was developed on hospital day 4. Substernal pain was aggravated and dyspnea developed in the supine position on hospital day 6. Chest radiograph showed cardiomegaly and subsegmental atelectasis on both lower lungs on hospital day 8. He was transferred to a university hospital on hospital day 9 because ST segment was elevated on ECG and cardiac enzymes, such as creatine phosphokinase (CPK), creatine kinase-MB (CK-MB), and troponin, were increased. Cardiac enzymes at the university hospital on the same day were CPK 5179 IU/l, CK-MB 142 ng/ml, myoglobin 491 ng/ml, troponin-I 28.2 ng/ml (Table 1), and ECG revealed ST segment elevation and T-wave inversion on from V2 to V6 (Fig. 1). Transthoracic echocardiography (TTE) on hospital day 10 showed global hypokinesia of left ventricle (LV) with further decreased wall motion of the left circumflex artery (LCX) territory and severe LV systolic dysfunction (ejection fraction (EF) 20%) (Fig. 2). Tl/Tc myocardial SPECT on next day revealed reversible ischemia. Coronary angiography that performed on hospital day 23 to exclude ischemic cardiomyopathy showed no significant luminal narrowing of coronary arteries. He had no neurological symptoms and the cardiac enzymes
were normalized and ECG revealed normalized ST segment with delta wave that he had had primarily (Fig. 1) after he was treated conservatively with ACE inhibitor and diuretics. He was discharged with no remarkable symptoms except decreased cardiac function on hospital day 23 (Table 1).

The Korea Occupational Safety and Health Agency (KOSHA) reported that the air concentration of hydrogen sulfide was 68 ppm (OSHA ceiling level is 20 ppm) and the levels of other gases were all normal (carbon monoxide 2 ppm, methane lesser <1%, oxygen normal) at the accident point, 4 m below ground, 2 days after the accident. The results of air monitoring and the rotten-egg smell at the scene supported the diagnosis of dilated cardiomyopathy induced by hydrogen sulfide.

At 6 mo follow up, chest X-ray showed no cardiomegaly (Fig. 2) and TTE revealed improved global LV systolic function (EF 45%) with reduced LV chamber size. Dyspnea on exertion had been somewhat improved, but was still sustained after 6 mo.

**Discussion**

The rotten-egg smell at the scene and the exceeding hydrogen sulfide level in the manhole over three-fold of OSHA ceiling level indicate that the immediate collapse was occurred due to hydrogen sulfide inhalation. The actual level of hydrogen sulfide in the manhole at the time of accident could be estimated to exceeding 700 ppm at least.

Hydrogen sulfide is inhaled and rapidly absorbed through respiratory membranes, and then acts as a mucus membrane irritant at low doses (<200 ppm) and as an cellular asphyxiant to the central nervous system and myocardium at high doses (>1,000 ppm). As an
intracellular toxin, it directly inhibits cytochrome oxidase and then disrupts electron transport in mitochondria. Inhibition of cytochrome oxidase leads to significantly anaerobic metabolism, severely decreased adenosine triphosphate (ATP) production with curtailed cellular energy generation, and the generation of lactic acid. Nervous and cardiac tissues, which have the highest oxygen demand, are especially sensitive to the disruption of oxidative metabolism.

Myocardium need to maximum extract (75%) of available oxygen in blood even at resting state, due to continuous and high oxygen demand. So myocardium injury could be injured by increased oxygen demand and decreased oxygen supply. But hydrogen sulfide can cause myocardium injury despite of normal coronary blood flow, because it prevents myocardial cell form using oxygen for energy generation.

Elevated ST segment of the left precordial lead, elevated cardiac enzyme, increased LV chamber size, decreased left ventricular wall motion and EF supported diagnosis of dilated cardiomyopathy (DCMP). DCMP on our case could be estimated to be developed from myocardial necrosis due to inhibition of myocardial cellular respiration by hydrogen sulfide with increased oxygen demand resulted from regular tachycardia. Tachycardia induced cardiomyopathy could be ruled out, because his tachycardia was not severe (120/min) and he had no obstruction of coronary arteries despite of WPW syndrome. The young age of patient and normal coronary angiography could rule out other reasons such as coronary artery disease (CAD).

A few cases of myocardial damage after exposure of hydrogen sulfide has been reported. Massive myocardial necrosis after exposure to hydrogen sulfide (at >500 ppm for more than 40 min) confirmed through postmortem autopsy and two victims without autopsy, one of whom died following massive cardiogenic pulmonary edema and the other died of acute cardiac infarction two months after exposure to the gas has been described previously. Later two victims also presented abnormal ECG with elevated ST segment in the left precordial leads. One surviving case has shown abnormal ECG such as a posterolateral myocardial ischemic changes, which had returned to normal gradually.

Our case has shown relatively good prognosis without neurologic sequelae despite of high dose exposure. It is estimated that the relatively short exposure (<10 min) would be the reason for good prognosis.

Hydrogen sulfide in the body is detoxified rapidly by oxidation into sulfide or thiosulfate. Hemoglobin-bound oxygen in the bloodstream and liver enzymes were involved in this metabolism. Lethal toxicity can occur when the detoxification capacity is overwhelmed by a high concentration.

The most important phase of lifesaving intervention in hydrogen sulfide exposure is emergency management at the scene. Victims must immediately be moved away from the contaminated area to fresh air and oxygen and artificial respiration must be applied if necessary. Any rescuers must take self-contained breathing apparatus while rescuing victims. Antidotes such as amyl...
nitrite via inhalation and intravenous sodium nitrite should be applied to victims within several minutes of the exposure\(^{12, \ 14}\). But the role of antidote therapy is ambiguous. In animal models, nitrite-induced methemoglobin is beneficial only when methemoglobin exists before or immediately after sulfide exposure\(^{15, \ 16}\). The protective effect of methemoglobin appears to be due to enhanced detoxification of sulfide by oxidation\(^ {17}\) and not to the formation of a sulfide-methemoglobin complex, as was previously hypothesized\(^ {1, \ 18}\). Oxyhemoglobin (hemoglobin-bound oxygen) also can detoxify sulfide by catalyzing oxidation\(^ {17}\). So hyperbaric oxygenation (HBO) would be beneficial due to the increase of oxyhemoglobin and oxygen delivery to the tissues\(^ {6}\).

Some authors have reported that neurologic sequelae of hydrogen sulfide resulted not from a direct toxicity on central nervous system neurons, but rather, from an indirect effect of cardiotoxicity such as severe hypotension\(^ {19, \ 20}\). So immediate cardiopulmonary resuscitation and close evaluation for cardiac function including cardiac enzyme monitoring, ECG and TTE are important to prevent the delayed toxicity associated with high dose hydrogen sulfide exposures.

In conclusion, this case highlights the danger of rapid cardiac damage caused by hydrogen sulfide, and raises that close monitoring of cardiac function is essential for victims of hydrogen sulfide. And also, the education of sewer workers about the mandatory use of respiratory protector at the scene and increased hospital preparedness are all critical steps to prevent additional victims and ensure successful rescue.

References