症 例 報 告

Delayed myocardial injury following acute hydrogen sulfide intoxication

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——Summary——(Jpn J Clin Toxicol 2012 ; 26 : 44–48)

〔Introduction〕 Hydrogen sulfide is a toxic, colorless gas produced by decaying organic matter. Its toxic effects are due to blocking of cellular respiratory enzymes, leading to anoxia.

〔Case presentation〕 We report a 28-year-old man who attempted suicide using hydrogen sulfide gas. When the emergency service arrived, his friend was dead and the patient was unconscious. He received supportive treatment and survived. In this patient both skeletal muscle and myocardial injury was observed after hydrogen sulfide intoxication. Skeletal muscle damage occurred first, because enzymes peak consisted of creatine phosphokinase, aspartate aminotransferase, and myoglobin was observed on hospital day 4. Myocardial injury was apparent on hospital day 15, because the subsequent enzymes peak was comprised of cardiac enzymes and associated electrocardiographic abnormalities. On hospital day 3, myocardial injury was detected and it evolved over the next 3 weeks to recover completely.

〔Conclusion〕 The mechanisms of rhabdomyolysis and myocardial injury resulting from hydrogen sulfide poisoning are not known, but may be related to cellular anoxia or a direct toxic effect. This case highlights not only the risk of delayed cardiac damage, but also rhabdomyolysis, and emphasizes that careful monitoring of cardiac function and of the levels of skeletal muscle-related enzymes is essential for victims of hydrogen sulfide poisoning.

Key words：rhabdomyolysis, nuclear medicine, suicide, myocardial injury, hydrogen sulfide

Introduction

Hydrogen sulfide (H_2S) is a colorless, heavier-than-air, inflammable, highly toxic irritant and chemically asphyxiant gas, which has a characteristic rotten egg odor[1]. Most cases of H_2S intoxication used to involve occupational exposure for workers involved in sewer maintenance, chemical manufacturing, and oil production[2)3)]. However, the number of suicides committed with H_2S has increased in Japan recently because of the increased availability of information pertaining to this gas on the Internet[4]. Concentrations of H_2S above 1,000 ppm are usually fatal after a few minutes, with a few breaths at this concentration leading to sudden loss of consciousness and death[1]. The mechanism of H_2S toxicity is similar to that of cyanide, which involves inactivation of cytochrome oxidase in the mitochondria that prevents cellular metabolism of oxygen[5]. Via this mechanism, H_2S induces brain damage and hypoxic myocardial dam-

age as well as mucosal irritation[5)6)]. The present report provides the results of cardiac testing, together with cardiac morphological and functional imaging, and level of skeletal muscle-related enzymes, in a man who recovered from H_2S poisoning after attempting suicide.

Case presentation

This study was approved by our investigational review board.

A 28-year-old man planned to commit suicide with his friend in a storeroom by inhaling H_2S, which was generated by mixing a hydrochloric acid-based detergent and sulfur-based bath soap. Before making this suicide attempt, he called colleagues to inform them. When the emergency service arrived, his friend was already dead and the patient was unconscious. Although the exact interval between suicide attempt and the emergency service arrival was unclear, it was estimated to be about 6 hours and the specific odor for H_2S was already absent. He was immediately transported to an emergency medical center. At presentation, he was unconscious with no spontaneous eye opening. There was no withdrawal of his extremities in response to pain. He had labored respiration and a persistent cough. The Glasgow coma scale (GCS) was 5/15, respiration rate was 36/min, blood pressure was 142/83 mmHg, pulse was 101/min, temperature was 37.6 ℃, and peripheral oxygen saturation was 95% (with oxygen via a mask at 10 L/min in the emergency room). Arterial blood gas analysis revealed a pH of 7.425, PO_2 of 222 mmHg, PCO_2 of 35 mmHg, carboxyhemoglobin of 2.8%, and bicarbonate of 22.8 mEq/L. Serum chemistry showed mildly elevated muscle enzymes (creatine phosphokinase (CPK) was 375 IU/L and myoglobin was 139 ng/mL), with normal renal function tests and electrolytes. Hematology tests showed a white blood cell count of 17,700/μL, hematocrit of 38%, and platelet count of 198,000/μL. The levels of glucose, blood urea nitrogen, creatinine, sodium, potassium, ionized calcium, and coagulation studies were within normal limits. Neurological function showed gradual improvement and he complained of anterior chest pain, a sore throat, and headache. Electrocardiograms were recorded on admission and in the ICU, but were unremarkable (Fig. 1). Five hours after admission to ICU, his GCS was 14/15 and it was 15/15 on hospital day 3. In addition to supportive care, he also received hydration. Renal function remained normal. The levels of CPK, aspartate aminotransferase (AST), and myoglobin respectively peaked at 7,203 IU/L, 217 IU/L, and 723 ng/mL on hospital day 4, and then decreased (Fig. 2). The CPK-MB isoenzyme fraction reached a maximum of 118 ng/mL and troponin I reached a maximum of 3 ng/mL on hospital days 10 and 12, respectively (Fig. 2). On hospital day 3, the electrocardiogram (ECG) revealed ST segment elevation in leads I, II, III, aV_F, V5, and V6, as well as Q waves in leads III and aV_F. On hospital day 12, the ECG revealed normalization of the ST segment, but Q waves persisted in leads III and aV_F (Fig. 1).

Transthoracic echocardiography was done on hospital day 7 and cardiac magnetic resonance imaging was performed on day 9 but the findings were unremarkable. On day 12, to clarify the reason for the sustained elevation of cardiac enzymes, we performed cardiac nuclear imaging and measured the uptake of ^{99m}Tc-tetrofosmin and beta-methyl-p-(^{123}I) iodophenyl pentadecanoic acid to assess myocardial blood flow and myocardial fatty acid metabolism, respectively. However, the cardiac nuclear findings were unremarkable. He was discharged with no symptoms on hospital day 28.

Discussion

In this patient both skeletal muscle and myocardial injury was observed after H_2S intoxication. Skeletal muscle injury occurred first, and myocardial injury

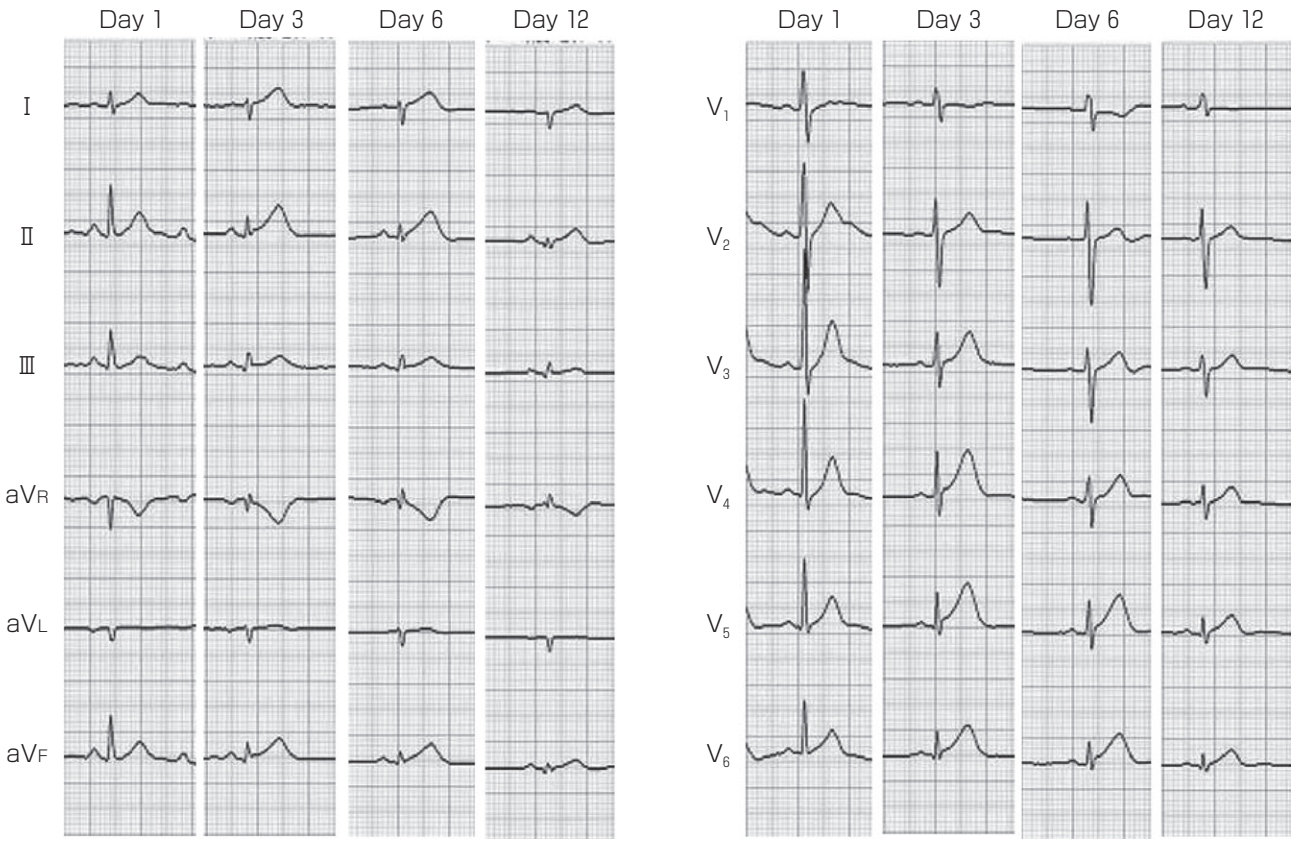

Fig. 1 Electrocardiogram（ECG）changes
On hospital day 3, the ECG revealed ST segment elevation in leads I, II, III, aVF, V_5, and V_6, as well as Q waves in leads III and aVF. On hospital day 12, the ECG revealed normalization of the ST segment, but Q waves persisted in leads III and aVF.

was apparent on hospital day 15.

A few cases of delayed myocardial damage after exposure to H_2S had been reported. One person died of acute myocardial infarction at two months after exposure to this gas[6]. Inoue et al reported two cases of H_2S poisoning with delayed lethal myocardial injury[7]. A patient developed dilated cardiomyopathy 9 days after H_2S inhalation, associated with ECG changes and elevation of cardiac enzymes[8]. Other survivors also have shown delayed myocardial damage with transient abnormalities of the ECG and cardiac contractility[9)10)]. The myocardium has a very high oxygen requirement and thus is thought to be sensitive to the disruption of oxidative metabolism[11]. Binding of H_2S to mitochondrial cytochrome *c* oxidase slows oxidative phosphorylation and causes myocardial hypoxia[5]. However, the reason for delayed appearance of cardiac injury after exposure to H_2S is not apparent. It could be suggested that cardiac injury due to H_2S inhalation is not only related to local hypoxia, but also to selective organ toxicity for the myocardium, but further study is needed to clarify this point.

As far as we know, this is the first report of rhabdomyolysis associated with H_2S intoxication. H_2S has a mechanism of action similar to that of cyanide and it affects metallo-enzymes, particularly mitochondrial cytochrome oxidase, thereby preventing cells from metabolizing oxygen[5]. The mechanism of rhabdomyolysis resulting from H_2S poisoning is unknown, but it may be related to cellular anoxia or a direct toxic effect. The impaired consciousness observed in our patient could have promoted rhabdomyolysis by pressure-induced ischemia due to prolonged immobilization and muscle compression. Possible unwitnessed seizures may also have contributed to skeletal muscle breakdown.

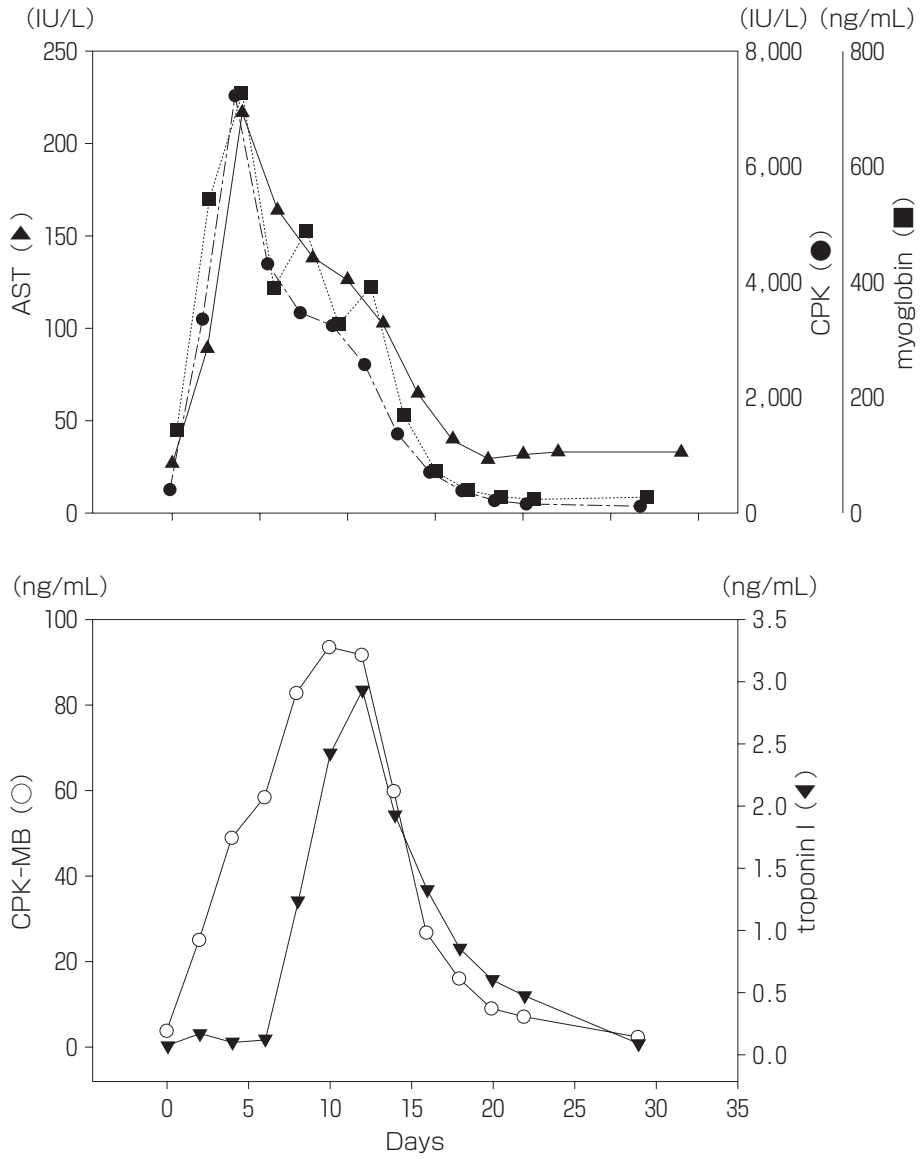

Fig. 2 Changes in the plasma levels of various muscle enzymes

Conclusion

This patient displayed skeletal muscle injury being followed by myocardial injury after acute H_2S intoxication. This report highlights not only the risk of delayed cardiac damage, but also rhabdomyolysis, and emphasizes that careful monitoring of cardiac function and of the levels of skeletal muscle-related enzymes is essential for victims of H_2S poisoning.

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要旨

はじめに：硫化水素は有機物の分解過程で発生する無色の有毒ガスで，細胞呼吸鎖を遮断し組織低酸素血症を惹起する。

症例：硫化水素ガスによる 28 歳，男性の自殺企図症例を報告する。救急隊現着時に友人は死亡しており，患者は昏睡状態で発見された。搬送後，ICU に入室，全身状態は徐々に改善し第 28 病日に軽快退院した。経過中，横紋筋融解症と心筋障害を認めた。血中 CPK，ALT，ミオグロビンが第 4 病日にピークを認めたことより横紋筋融解症の先行が示唆された。第 15 病日にピークを認め 3 週間継続した心筋逸脱酵素上昇は心電図変化を伴っており，遅発性心筋障害を示唆した。

まとめ：硫化水素中毒による横紋筋融解症，心筋障害の発生機序は明らかでないが，組織低酸素もしくは筋細胞に対する直接的毒性の関与が推察される。硫化水素中毒患者では横紋筋融解症，遅発性心筋障害の発生に留意し心筋機能，筋逸脱酵素のモニタリングが肝要である。