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CASE REPORT

ADVANCED

HEART CARE TEAM/MULTIDISCIPLINARY TEAM LIVE

Prolonged Cardiogenic Shock Due to Hydrogen Sulfide Intoxication Requiring Long-Term Venoarterial Extracorporeal Membrane Support

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ABSTRACT

We describe a case of severe biventricular failure and cardiovascular collapse following exposure to the manure gas hydrogen sulfide. Initial tests indicated uncoupling of cellular bioenergetics in addition to myocardial damage. Cardiopulmonary support with venoarterial extracorporeal membrane oxygenation was initiated, and the patient could be successfully weaned from support after 28 days. (**Level of Difficulty: Advanced.**) (J Am Coll Cardiol Case Rep 2022;4:1389–1393) © 2022 The Authors. Published by Elsevier on behalf of the American College of Cardiology Foundation. This is an open access article under the CC BY-NC-ND license (http://creativecommons.org/licenses/by-nc-nd/4.0/).

CLINICAL SUMMARY

A 25-year-old healthy male agricultural worker lost consciousness while cleaning inside an empty manure pit. After 15 minutes inside the pit, the patient was rescued by a colleague who also collapsed shortly after getting out of the manure pit. During initial on-site resuscitation, the patient remained unresponsive and hyperventilating. The initial blood pressure was 200/110 mm Hg, heart rate was 140 beats/min, and peripheral oxygen saturation (Spo_2) was 90%. The patient was intubated following a generalized seizure treated with midazolam. Point-of-care ultrasound revealed severely reduced left ventricular (LV) ejection fraction (LVEF) of 20%. During transportation to the emergency department, the patient became hypotensive and required high-dose vasopressor agents.

On arrival at the emergency department, acute pulmonary edema and reactive pneumonitis developed, as evident on a computed tomography scan. Mild hypoxemia persisted, with an Spo_2 of 91% despite mechanical ventilation with high positive end-expiratory pressure and 100% oxygen. An arterial blood gas analysis showed metabolic acidosis with a

LEARNING OBJECTIVES

- To comprehend the clinical appearance, pathophysiology, and treatment of H_2S-induced cardiogenic shock following manure gas exposure.
- To highlight possible long-term cardiovascular outcomes from H_2S cardiotoxicity.

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ABBREVIATIONS AND ACRONYMS

ECG = electrocardiogram

H_2S = hydrogen sulfide

HBOT = hyperbaric oxygen therapy

LV = left ventricular

LVEF = left ventricular ejection fraction

PEA = pulseless electrical activity

PCWP = pulmonary capillary wedge pressure

RV = right ventricular

Spo_2 = peripheral oxygen saturation

Svo_2 = central venous oxygen saturation

TAPSE = tricuspid annular plane systolic excursion

VA-ECMO = venoarterial extracorporeal membrane oxygenation

lactate level of 8.0 mmol/L (Table 1). Methemoglobinemia was not present. Hypotension resulting from a combination of vasodilatation and biventricular cardiac failure persisted, and the electrocardiogram (ECG) demonstrated sinus tachycardia with a heart rate of 130 beats/min and universal ST-segment elevations (Figure 1). Bronchoscopy findings were unremarkable. Initially, his body temperature was 34.7 °C (94.5 °F).

The rescuing colleague had bilateral conjunctivitis; however, the colleague quickly recovered with no cardiopulmonary symptoms.

QUESTION 1: WHICH ARE THE DIFFERENTIAL DIAGNOSES, AND WHICH TOXIC EXPOSURES SHOULD BE SUSPECTED?

Hydrogen sulfide (H_2S) intoxication was suspected. Exposure to other manure gasses was also considered, and hypoxia resulting from aspiration, asphyxia, or central nervous system depression could not be ruled out.

Manure pits are known to produce hazardous gases, of which H_2S is known as one of the most lethal.[1] Exposure to low doses may result in corneal inflammation, respiratory tract irritation, and toxic pulmonary edema. The diagnosis is made on the basis of the clinical presentation because H_2S rapidly dissipates from the blood and tissues and therefore cannot easily be measured.[1] High concentrations of inhaled H_2S lead to hyperpnea, followed by unconsciousness, and subsequently apnea, eventually leading to cardiac arrest. In addition to cerebral and respiratory decline, H_2S toxicity may involve cardiocirculatory failure.[2,3] Importantly, H_2S can reduce cardiac contractility and cause rapid hemodynamic deterioration leading to pulseless electrical activity (PEA).[3]

TABLE 1 Blood Samples During Hospital Admission

	Day 0	Day 1	Day 2	Day 3	Day 7	Day 28	Day 49
Lactate, mmol/L	8.0	>15	11.8	5.1	3.1	3.8	1.5
Troponin I, ng/L	N/A	N/A	81,429	50,736	23,359	581	N/A
Alanine aminotransferase, U/L	26	501	3,898	5,206	1,653	36	23
Creatinine, μmol/L	88[a]	160[a]	227[a]	207[a]	193[a]	126[a]	119
Bilirubin, μmol/L	7	33	64	90	63	136	27

[a]During continuous renal replacement therapy.
N/A = not available.

QUESTION 2: WHICH ARE THE NEXT STEPS IN THE MANAGEMENT OF THIS PATIENT?

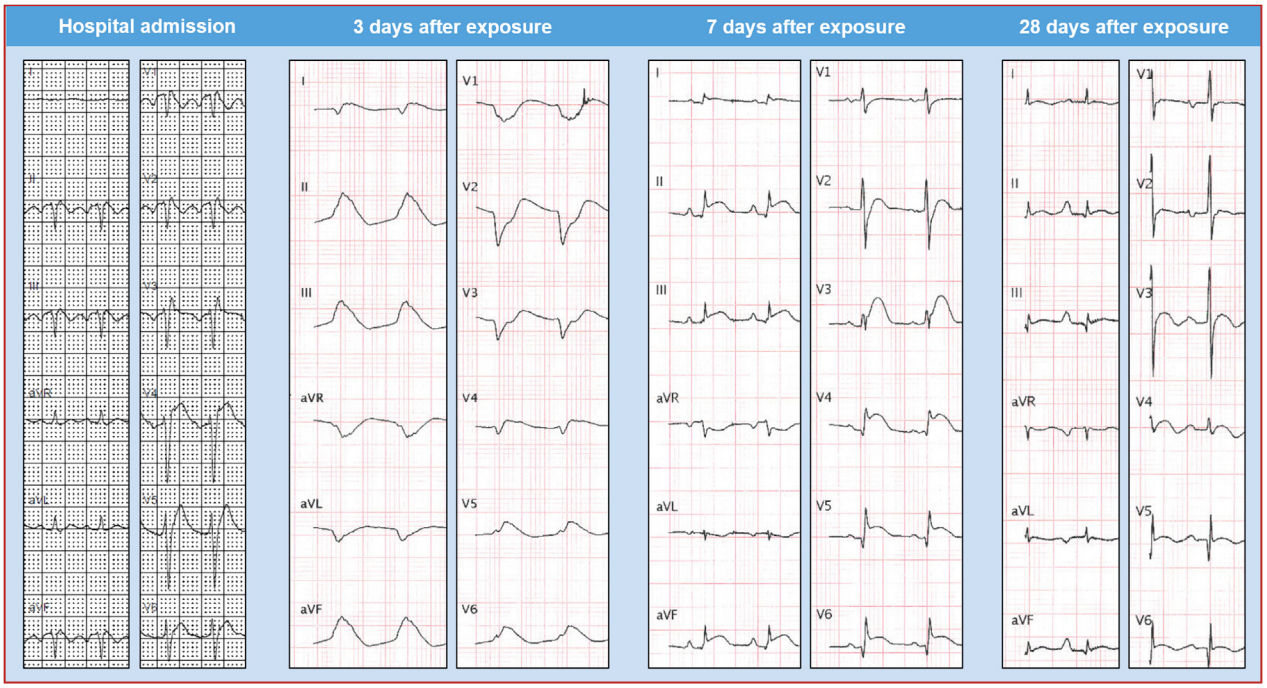
Treatment options for H_2S intoxication remain scarce and are based on experimental data, anecdotal reports, and pathophysiologic rationale. Notably, sulfide is rapidly cleared from the circulation; hence, treatment with scavengers such as nitrite or thiosulfate is believed to be effective only in the very initial phase of exposure.[1] Hyperbaric oxygen therapy (HBOT) has been suggested as a logical treatment option to increase oxygen availability to the anoxic tissues.[4] Hydroxocobalamin and methylene blue have also proven beneficial in animal studies.[3,5]

The patient was rewarmed and physically decontaminated. While still intubated, he received 2 consecutive 90-minute treatments of HBOT. In addition, high-dose hydroxocobalamin was administered. Sodium nitrite and methylene blue were not available during the initial resuscitation and were therefore not administered. During the second HBOT treatment, hemodynamics deteriorated, and PEA was soon evident. Cardiopulmonary resuscitation was immediately initiated, and the patient had intermittent return of spontaneous circulation with in-between episodes of both asystole and ventricular tachycardia. After 40 minutes of resuscitation, a venoarterial (VA) extracorporeal membrane oxygenation (ECMO) (VA-ECMO) circuit was implanted; then, circulation was reestablished. The right femoral artery (21-F) and vein (23-F) were cannulated, including an 8-F arterial distal shunt. The ECMO circuit was couplet to a Quadrox-I oxygenator (Getinge).

Despite high-dose infusions with norepinephrine, epinephrine, vasopressin, and milrinone, mean arterial blood pressure was increased only to 60 mm Hg, with near absence of arterial line waveform upstrokes. Severe biventricular failure was evident; at full ECMO flow (3.5 L/min), LVEF was 5%, and tricuspid annular plane systolic excursion (TAPSE) was 3 mm (Videos 1A to 1C). Kidney and liver failure was also apparent, with a need for continuous renal replacement therapy (Table 1). After 24 hours, lactate levels were higher than the upper detection limit (>15 mmol/L) (Table 1). Spo_2 and central venous oxygen saturation (Svo_2) were 99% and 68%, respectively.

On day 3, the ECG demonstrated bizarre broad QRS complexes (Figure 1), and high-sensitivity troponin values were exceedingly elevated (Table 1). Despite severely deranged hemodynamics, Svo_2 remained paradoxically elevated at 70% (Table 2).

FIGURE 1 Electrocardiograms During Hospital Admission



QUESTION 3: WHICH PATHOPHYSIOLOGICAL MECHANISMS COULD EXPLAIN THE ELEVATED LEVELS OF LACTATE AND TROPONINS IN COMBINATION WITH THE HIGH SVO_2?

H_2S is a cellular asphyxiant that blocks mitochondrial respiration by reversibly binding to and inhibiting the cytochrome *c* oxidase (mitochondrial complex IV).[1] Because of blockage of aerobic metabolism, accelerated anaerobic glycolysis leads to lactic acidosis. Proglycolytic effects of epinephrine and peripheral hypoperfusion may further amplify this process. In addition, similar to cyanide toxicity, blockage of tissular oxygen use may increase Svo_2.[6] Indeed, we discovered unmeasurably high lactate levels on day 1, accompanied with a paradoxically elevated Svo_2 at 70% compatible with deranged mitochondrial oxidative metabolism and increased anaerobic glycolysis. Moreover, excessive formation of reactive oxygen species can generate apoptosis and mitochondrial damage.[7] In combination with cellular energy deprivation, these processes may lead to severe myocardial damage, reflected by myocardial dysfunction and elevated troponin values.

TABLE 2 Hemodynamic Parameters During Hospital Admission

	Day 3	Day 7	Day 28 on VA-ECMO	Day 28 Weaned From VA-ECMO	Day 49 on Ward
Central venous pressure, mm Hg	22	20	20	25	1
Pulmonary arterial pressure, mm Hg	35/28 (31)	28/23 (25)	36/13 (25)	30/17 (26)	24/0 (8)
Pulmonary capillary wedge pressure, mm Hg	17	16	15	16	4
Cardiac index, L/min/m^2	2.0	2.0	2.8	2.5	3.8
Central venous saturation, %	70	66	76	64	71
Blood pressure, mm Hg	78/75 (77)	73/65 (67)	97/73 (64)	90/52 (67)	90/49 (63)
Extracorporeal membrane support flow, L/min	3.5	3.2	3.5		

VA-ECMO = venoarterial extracorporeal membrane oxygenation.

QUESTION 4: WHAT COULD EXPLAIN THE PATHOLOGIC ECG FINDINGS ON DAY 3?

The ECG on day 3 resembled a sine wave pattern, although electrolytes were within normal values. H_2S intoxication is known to involve inhibition of L-type calcium (Ca^{2+})-channel activity.[5] This negative inotropic effect resembles a calcium-channel blocker overdose; that is, suppressed myocardial excitation-contraction coupling in addition to hampered cardiac conduction and vascular relaxation. Indeed, serial ECGs demonstrated severe conduction abnormalities during the initial days that may have resulted from severe myocardial damage and energy deprivation in combination with calcium-channel blockage.

QUESTION 5: TREATMENT WITH VA-ECMO MAINTAINS CARDIOPULMONARY SUPPORT AT THE COST OF INCREASED LV AFTERLOAD. WHEN AND HOW SHOULD LV UNLOADING BE CONSIDERED?

LV unloading or venting strategies may be indicated if LV distention and pulmonary edema are evident.[8] Reduced arterial pulse pressure and echocardiographic evidence of scarce aortic valve opening are important measures to assess LV overload during VA-ECMO treatment. More importantly, increased pulmonary capillary wedge pressure (PCWP) may indicate deleterious increments in LV end-diastolic pressure. Therefore, LV distention and increased PCWP should lead to consideration about some form of LV unloading strategy. Several unloading strategies have been described.[8] Reducing ECMO flow in combination with inotropic agents may improve aortic valve opening, albeit at a cost of reduced circulatory support, limited LV unloading, and increased myocardial oxygen demand. In contrast, a transaortic ventricular assist device (eg, Impella, Abiomed) provides direct LV unloading by decompressing LV filling pressure.[8]

In the present case, echocardiography demonstrated persistent aortic valve opening during ECMO treatment. In addition, PCWP remained at approximately 16 mm Hg (**Table 2**), and the LV was not significantly dilated. Therefore, the current treatment strategy with VA-ECMO in combination with inotropic agents was continued. Heart transplantation was not an option given the patient's multiple fungal pulmonary and bloodstream infections. During the following week, lactate and troponin values declined, and vasopressor treatment could be reduced. Nonetheless, hemodynamics remained compromised, and there was a persistent need for full cardiopulmonary support with VA-ECMO flow of 3.2 L/min (**Table 2**). On day 7, ECG revealed narrowing of the QRS complexes and persistent ST-segment elevations (**Figure 1**). After 4 weeks of VA-ECMO treatment, LVEF was slowly improving to 15% (Video 2A). The ST-segment elevations nearly vanished (**Figure 1**). Even so, severe right ventricular (RV) dysfunction persisted (Video 2B), and several weaning attempts from VA-ECMO were unsuccessful because of elevated central venous pressure and compromised cardiac output.

QUESTION 6: WHICH TREATMENT STRATEGIES COULD IMPROVE THE HEMODYNAMIC STATUS IN THE PURSUIT TO WEAN THIS PATIENT FROM VA-ECMO?

Because RV dysfunction remained problematic, the patient was treated with aggressive fluid removal and inhaled nitric oxide. In addition, sildenafil was added to the treatment. On day 28, the patient was successfully weaned from VA-ECMO with acceptable hemodynamics (**Table 2**). During week 5, the patient was weaned from mechanical ventilation and was now fully conscious. LVEF improved to 25%, and TAPSE improved to 10 mm (Videos 3A and 3B). After 6 weeks, the patient was fully mobilized for the first time since admission. Invasive hemodynamic values were significantly improved (**Table 2**).

After 85 days of admission, the patient was discharged to a recovery facility. Complications of intensive care unit-acquired weakness were evident, and the patient had Parinaud syndrome with double vision because of a thalamic infarction. No other ECMO-related complications occurred. Cognition, as assessed by the Montreal Cognitive Assessment test, was fully intact, and he slowly regained functional ability. Lung, liver, and kidney function also recovered. Therapy for chronic heart failure was titrated to maximal tolerable doses; however, biventricular failure persisted; LVEF was 40%, and TAPSE was 12 mm. The patient is currently being followed up in a heart failure outpatient clinic.

CONCLUSIONS

H_2S intoxication from manure gas exposure can cause severe cardiovascular collapse along with persistent heart failure. With adequate cardiopulmonary resuscitation, cerebral injury may be prevented. In this case report of severe cardiogenic shock following H_2S

exposure, we illuminate that long-term mechanical support should be considered because it can be lifesaving.

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APPENDIX For supplemental videos, please see the online version of this article.

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