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■증 례■

A Case of Uremic Pericarditis and Cardiac Tamponade That Developed after Ethylene Glycol Poisoning

－A Case Report－

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Ethylene glycol is commonly incorporated into automotive antifreeze agents and a variety of other commercial products. Ethylene glycol poisoning can cause life-threatening metabolic acidosis, cardiopulmonary failure, and renal failure that may be fatal. We present an unusual case of a patient who ingested a large amount of ethylene glycol for the purpose of suicide and developed multiorgan damage, including acute renal failure followed by uremic pericarditis and cardiac tamponade. This unusual complication was effectively managed with echocardiography-guided percutaneous pericardiocentesis and continuous catheter drainage for 3 days. After intensive hemodialysis and supportive care, the patient made a good recovery with near normal cardiac and renal function. Physicians should be aware of the possibility of acute pericarditis and cardiac tamponade in cases of acute renal failure caused by ethylene glycol poisoning.

Key Words: uremic pericarditis, cardiac tamponade, ethylene glycol, acute renal failure.

Ethylene glycol is a colorless, odorless, water-soluble, and sweet tasting compound that is used as an antifreeze in car radiators and as a chemical solvent.[1,2] Ethylene glycol is reported as a common cause of poisoning, either accidental or in a suicide attempt, all over the world because of its easy accessibility and widespread use.[1] Ethylene glycol itself is not toxic until metabolized, but many metabolites of ethylene glycol are very toxic and may be lethal. The classic presentation of ethylene glycol poisoning includes neurological features, such as convulsions and focal neurological abnormalities culminating in coma, followed by development of profound metabolic acidosis, cardiopulmonary failure, and oliguric renal failure. We recently treated a 29-year-old woman who had ingested a massive amount of ethylene glycol. She experienced severe toxic effects, including neurological symptoms, metabolic acidosis, cardiopulmonary failure, and acute renal failure, followed by uremic pericarditis and cardiac tamponade. However, she was successfully treated with good recovery of cardiac and renal function.

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CASE REPORT

A 29-year-old woman who had been experiencing nausea, vomiting, somnolence, ataxia, and confusion for 6 hr visited the emergency room; she had no medical history of disease. On physical examination, she was found to be disoriented and breathless at rest and had peripheral cyanosis and cold extremities. There was no evidence of trauma. The patient had round, equal, contracted pupils and a supple neck, and she could spontaneously move all 4 limbs. Her vital signs were as follows: blood pressure, 110/70 mmHg; heart rate, 120 beats/min; and respiratory rate, 28 breaths/min. The cardiac monitor showed sinus rhythm. The oxygen saturation was 96% on oxygen supplementation, 2 L/min by nasal cannula and the fingerstick glucose value was 167 mg/dl.

The patient's mother arrived at the emergency room 20 min after the patient's arrival and brought an empty automotive antifreeze bottle (500 ml capacity) that was found in the patient's room. No other drugs or alcohol was thought to have

been ingested. Massive voluntary ethylene glycol poisoning was immediately suspected. Later, after the patient became mentally alert, she stated that she had ingested 500 ml of the antifreeze 12 hr before her visit to the hospital.

Investigation revealed the following results: hemoglobin level, 16.8 g/dl; white blood cell count, 25,700/mm^3 (neutrophils, 85%; lymphocytes, 12%); and platelet count, 398,000/mm^3. The results for the arterial blood gas analysis were as follows: pH 6.838; partial pressure of carbon dioxide in arterial blood (Pa_{CO2}), 10.8 mmHg; partial pressure of oxygen in arterial blood (Pa_{O2}), 142 mmHg; HCO_3^-, 1.8 mmol/L; and O_2 saturation, 96.3%. The serum biochemistry results were as follows: sodium level, 142 mEq/L; potassium level, 6.85 mEq/L; chloride level, 107 mEq/L; calcium level, 10.3 mg/dl; phosphorus level, 8.7 mg/dl; blood urea nitrogen level, 21.0 mg/dl; and creatinine level, 1.76 mg/dl. The measured anion gap was 33 mEq/L. The serum osmolality was 382 mOsm/kg, with an osmolar gap of 81 mOsm/kg. Numerous calcium oxalate crystals were seen on urine microscopy. The chest radiograph showed normal appearance without evidence of pulmonary edema, and the electrocardiogram showed sinus tachycardia with a heart rate of 130 beats/min and tall peaked T waves in precordial leads (Fig. 1A).

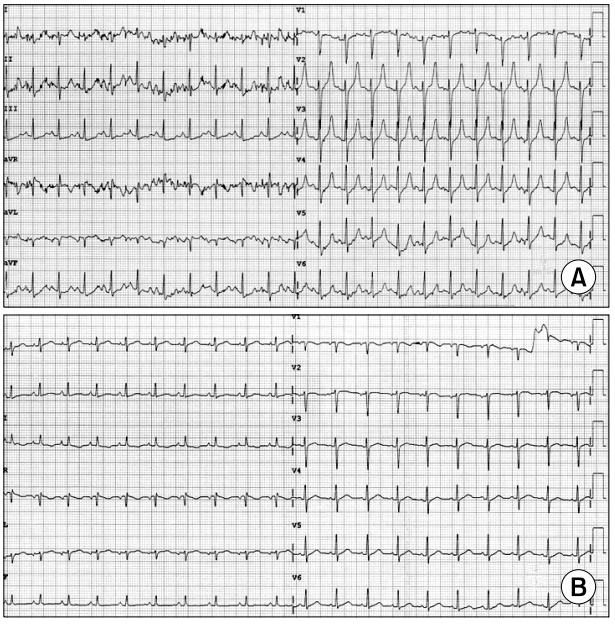

Fig. 1. Electrocardiogram showed sinus tachycardia (130 beats/min) with tall peaked T waves in precordial leads (A). Electrocardiogram showed sinus tachycardia (120 beats/min) with low QRS voltage tendency in limb leads and T-wave inversions in leads III, aVF (B).

Treatment for acute ethylene glycol poisoning was started with an intravenous infusion of 100% dehydrated ethanol at a loading dose of 0.8 g/kg over 30 minutes, followed by an infusion rate of 100 mg/kg/hr. The severe metabolic acidosis was corrected with a continuous infusion of bicarbonate. The patient was transferred to the medical intensive care unit and emergency hemodialysis was started approximately 6 hr after she arrived at the emergency room. During the first hemodialysis session, the patient's blood pressure dropped to 70/50 mmHg, and she was unresponsive to painful stimuli. The hemodialysis was stopped, and a continuous intravenous infusion of dopamine was started. She was intubated and mechanical ventilation was initiated. Continuous venovenous hemodiafiltration (CVVHDF) was started after her blood pressure recovered to 120/80 mmHg.

She became completely anuric by the 10th hospital day and

Table 1. Serial Laboratory Data during the Hospital Course

	pH	$PaCO_2$ (mmHg)	PaO_2 (mmHg)	BE (mmol/L)	HCO_3^- (mmol/L)	BUN (mg/dl)	Creatinine (mg/dl)	Sodium (mEq/L)	Potassium (mEq/L)
Admission	6.838	10.8	142.8	−31.1	1.8	21.0	1.7	142	6.8
6 hr*	6.850	11.1	148.5	−30.8	1.9			145	5.2
12 hr	7.293	21.2	139.6	−14.1	10.0			139	4.2
18 hr	7.344	17.5	179.7	−13.5	9.3	11.2	1.5	138	2.9
48 hr	7.427	34.5	70.4	−1.4	22.2	7.0	1.0	136	3.5
4 day	7.452	29.0	114.6	−2.5	19.8	41.0	2.0	132	3.0
7 day	7.458	26.7	116.7	−3.7	18.5	60.0	2.0	133	3.0
14 day†	7.458	36.9	101.3	1.9	25.5	44.4	1.1	147	3.5
16 day	7.404	33.9	123.9	−3.1	20.7	131.8§	3.8	145	3.8
18 day‡	7.424	29.3	93.6	−4.4	18.8	119.5	4.1§	139	4.1
23 day						57.6	2.2	135	3.3
31 day	7.491	37.7	81.4	4.7	28.2	16.1	1.0	139	3.2

*Hemodialysis was started; †Dialysis was changed to intermittent hemodialysis; ‡Cardiac tamponade developed; §Peak level of each data.

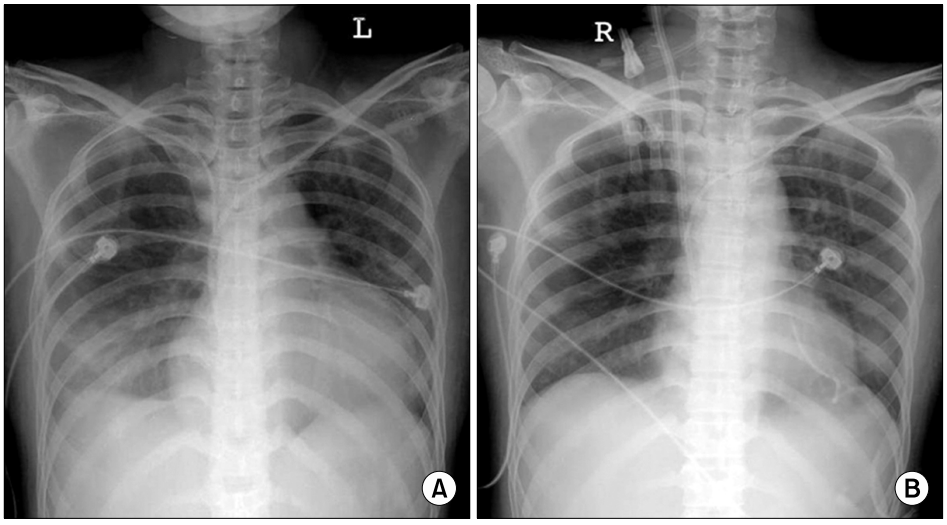

Fig. 2. Chest radiograph showed water-bottle shape cardiomegaly (cardiothoracic ratio 64%) before pericardiocentesis (A). Chest radiograph showed improvement of cardiomegaly (cardiothoracic ratio 51%) after pericardiocentesis (B).

exhibited elevation in the creatinine and blood urea nitrogen levels with peak values of 4.1 mg/dl and 131.8 mg/dl, respectively (Table 1). CVVHDF was continued, and she remained on an ethanol infusion (100－150 mg/dl) throughout the dialysis. After the procedures, her vital signs, acid-base balance, and electrolyte balance stabilized. She became mentally alert and was extubated on the 13th hospital day. Urine production started on the 14th hospital day, and a urine output of ＞500 ml/day was obtained; the dialysis protocol was changed from CVVHDF to intermittent hemodialysis three times per week (on alternate days except Sunday).

On the 18th hospital day, she complained of chest pain, which was worse in the recumbent position, dry cough, and dyspnea. Her vital signs were as follows: blood pressure, 100/60 mmHg; heart rate, 120 beats/min; respiratory rate, 30 breaths/min; and body temperature, 37.7°C. Physical examination revealed muffled heart sound, jugular venous distension, and crackle from both lungs. The chest radiograph showed water bottle-shaped cardiomegaly (Fig. 2), which was absent in the previous radiograph, and the electrocardiogram showed sinus tachycardia (120 beats/min) with low QRS voltage and T wave inversions in leads III, aVF (Fig. 1B). The serum blood urea nitrogen level was 119.5 mg/dl, and the creatinine level was 4.1 mg/dl. The serum cardiac enzyme study revealed that the MB fraction of creatinine phosphokinase (CK-MB) level (2.6 ng/ml) was within the normal range and the troponin I level (9.28 ng/ml) was elevated. Several hours later, the patient's blood pressure dropped to 80/50 mmHg and she required fluid resuscitation. Transthoracic echocardiography revealed an ejection fraction of 65%, normal left ventricular systolic function without any wall motion abnormality, and the presence of a large amount of pericardial effusion (Fig. 3A, B). Percutaneous pericardial catheter drainage was performed under the echocardiographic guidance for 3 days. In the first 24 hr, 700 ml of dark brown serous fluid was aspirated (Fig. 4). Pericardial fluid analysis provided the following results: protein level, 5.6 g/dl; albumin level, 2.8 g/dl; lactate dehydrogenase (LDH), 2329 IU/L; white blood cell count, 75/mm^3 (neutrophils, 65%; lymphocytes, 35%); glucose level, 85 mg/dl; and adenosine deaminase level (ADA), 8 IU/L. The tuberculosis (TB) polymerase chain reaction (PCR) results for the fluid were negative. No microorganism was isolated or cultured from the pericardial fluid. Cytologic examination of the pericardial fluid showed chronic inflammation. Uremic pericarditis with pericardial effusion followed by cardiac tamponade was suspected. Intensive hemodialysis was performed six times per week (every day except Sunday), resulting in normalization of the serum blood urea nitrogen and creatinine levels.

The patient was transferred to the general ward 27 days after admission. Serum biochemistry analysis showed that the blood urea nitrogen level was 16.1 mg/dl and the creatinine level was 1.0 mg/dl. The follow-up echocardiogram showed normal results, with no visible pericardial effusion and or hemodynamic instability (Fig. 3C, D).

DISCUSSION

Ethylene glycol is highly water-soluble, and it is rapidly absorbed from the gastrointestinal tract and quickly redistributed throughout the body.[2,3] Ethylene glycol is first hepatically metabolized to glycoaldehyde by alcohol dehydrogenase. Glycoal-

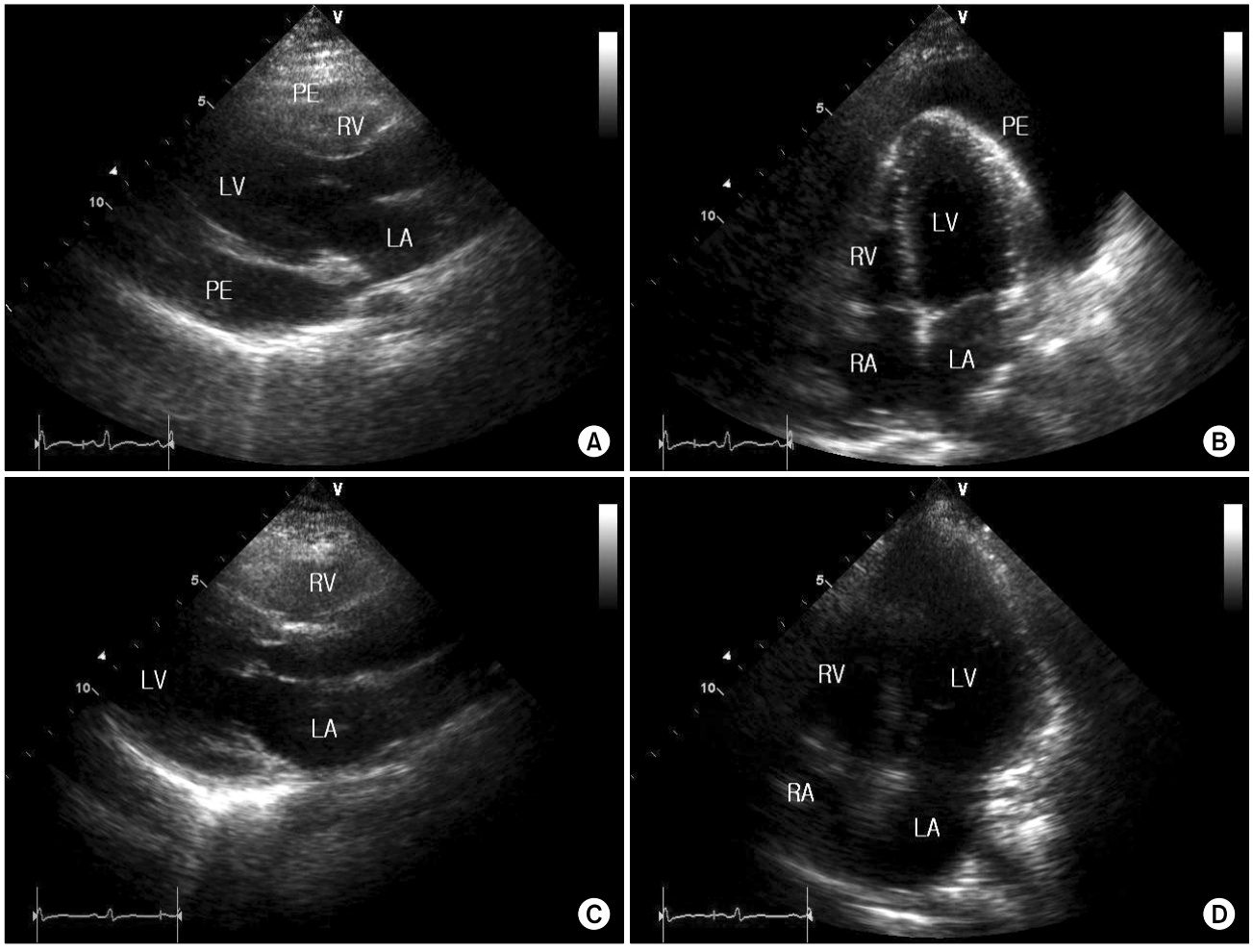

Fig. 3. Transthoracic echocardiographic two-dimensional images showed a large amount of pericardial effusion and diastolic collapse of the right ventricle in parasternal long axis and apical 4-chamber view (A, B). The follow-up images showed obvious improvement of the echocardiographic pattern (C, D). PE: pericardial effusion; RV: right ventricle; LV: left ventricle; RA: right atrium; LA: left atrium.

Fig. 4. Dark brown serous pericardial fluid was aspirated through echocardiography-guided pericardiocentesis.

dehyde is then oxidized to glycolic acid, glyoxylic acid, and finally to oxalic acid.[3] Oxalic acid precipitates with calcium to form calcium oxalate crystals. Ethylene glycol itself is not a toxic substance. However, the accumulation of toxic metabolites is responsible for the potentially fatal acidosis and renal failure that characterize ethylene glycol poisoning.[1] The peak plasma concentration is achieved 2－3 hr after oral ingestion, and the half-life of ethylene glycol is 3－10 hr.[3] The metabolites are detectable for up to several days, and calcium oxalate is detected in tissue for a much longer time, especially in the kidney.[2] The estimated lethal dose of ethylene glycol is 1.0－1.5 ml/kg, i.e., approximately 100 ml for an adult.[1,4]

The clinical syndrome of ethylene glycol poisoning involves 3 fairly distinct stages, depending on the time at which the different metabolites of ethylene glycol are formed.[3-8] The first stage is characterized by neurological manifestations, which oc-

cur between 30 min and 12 hr after ingestion of ethylene glycol. The patient may experience somnolence, disorientation, agitation, and confusion during this stage and may appear drunk without the odor of ethanol. Deeper central nervous system manifestations such as stupor, coma, convulsions, and focal or generalized seizures may develop during this stage. Gastrointestinal involvement, nausea, vomiting, and abdominal discomfort may also be observed. The second stage is characterized by profound metabolic acidosis with an elevated anion gap and the toxic effects of the various metabolites of ethylene glycol. Cardiopulmonary manifestations, such as heart failure and respiratory distress, occur 12－24 hr after ingestion and are caused by profound metabolic acidosis. Therefore, in this stage, virtually all the organ systems are affected, and multisystem failure may develop. Most deaths occur during the second stage.[3] The third stage is characterized by renal complications, which occur 24 hr after initial ingestion of ethylene glycol. Oliguric or anuric renal failure may last for up to 1 month or more.[9,10] Renal failure is typically acute and requires repeated hemodialysis.[11,12]

Our patient experienced several problems typically seen after ethylene glycol poisoning. After arrival at the emergency department, she complained of gastrointestinal manifestations such as nausea and vomiting and neurological symptoms such as somnolence, ataxia, and confusion. The patient developed cardiopulmonary decompensation 6 hr after she arrived at our hospital and required comprehensive care that included mechanical ventilation. She also developed severe metabolic acidosis and acute renal failure and required hemodialysis for more than 20 days.

In addition to the above symptoms, she developed acute pericarditis with pericardial effusion followed by cardiac tamponade. Pericardial fluid analysis revealed the presence of exudative effusion. The effusion was a dark brown serous fluid without evidence of malignancy or of bacterial or TB infection. Cytological examination of the pericardial fluid revealed only chronic inflammation. Although the patient underwent continuous hemodialysis after admission, her serum blood urea nitrogen and creatinine levels remained relatively high during this period. Therefore, renal replacement therapy was not completely effective in our patient, as reflected by the moderately elevated serum urea and creatinine levels. Retrospective review revealed that the serial chest radiographs taken from the 12th hospital day onward showed progressive cardiomegaly that may be correlated with acute pericarditis with pericardial effusion. Inadequate renal replacement therapy could potentially be related to the development of uremic pericardial effusion. Therefore, it is probable that more intense metabolic control, which can be achieved by intensive hemodialysis, is required in cases of acute renal failure that are slow to resolve, as was the case in our patient who ingested a massive amount of ethylene glycol.

Another interesting finding in our case was the development of pericarditis combined with subclinical myocarditis. The development of myocarditis after ethylene glycol poisoning was first reported in 1988.[5,13] Acute pericarditis is often accompanied by some degree of myocarditis.[14] In clinical practice both pericarditis and myocarditis coexist because they share common etiologic agents, such as viral infections, drugs, radiations, etc. The clinical presentation of pericarditis combined with myocarditis is varied, reflecting the variability of myocardial involvement.[14,15] Many cases may be subclinical and, in other patients, cardiac symptoms and signs are subtle. Symptomatic patients may complain of pleuritic chest pain, dyspnea, and palpitation. Cardiac enzyme elevations reflect myocardial lesion and provide a rough estimate of the extent of myocardial inflammation. Many clinicians consider an elevation in cardiac enzymes to be sufficient to diagnose myocarditis in patients with acute pericarditis.[14,15] Isolated elevations of troponin with normal CK-MB may reflect mildest degree of myocardial damage.[14] Electrocardiogram changes are common and these changes reflect some degree of myocardial involvement. Common findings are nonspecific T wave changes.[15] Echocardiography enables noninvasive detection of pericardial disease and impaired left ventricular systolic function.

Pleuritic chest pain and dyspnea were predominant symptoms with our patient, which were improved by percutaneous pericardial catheter drainage. These symptoms were mainly attributed by pericarditis with massive pericardial effusion. Significant ST segment changes were not observed at precordial leads, and T wave inversions in leads III, aVF were clinically insignificant. Echocardiography was performed to evaluate wall motions and left ventricular systolic functions of the heart. While the CK-MB level remained in the normal range, serum cardiac troponin I level was moderately elevated which led us to suspect subclinical myocarditis. However, certain drugs can cause pericarditis and myocarditis. There still remain small possibilities of ethylene glycol and its metabolites being causative agents of pericarditis and myocarditis.

The hospital course of our patient was complicated by cardiopulmonary failure, severe metabolic acidosis, and oliguric renal failure, followed by uremic pericarditis and cardiac tam-

ponade; however, she made a good recovery. This unusual case of uremic pericarditis and cardiac tamponade that developed after ethylene glycol poisoning was treated by echocardiography-guided pericardiocentesis with continuous catheter drainage and intensive hemodialysis. Physicians must be aware of the possibility of acute pericarditis and cardiac tamponade in cases of acute renal failure caused by ethylene glycol poisoning.

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