Korean J Leg Med 2017;41:137-140
https://doi.org/10.7580/kjlm.2017.41.4.137

Case Report

Death from Naphthalene Poisoning Manifesting as Toxic Hepatitis: An Autopsy Case

Jinhyuk Choi[1], Seong Hwan Park[1], Min Jee Park[2], Seok-Hoon Jeon[3]

[1]Department of Legal Medicine, Korea University College of Medicine, Seoul, Korea, [2]Division of Forensic Medicine, National Forensic Service, Seoul, Korea, [3]Seoul Clinic of Korea Forensic Investigation, Seoul, Korea

Received: October 20, 2017
Revised: October 31, 2017
Accepted: November 27, 2017

Correspondence to
Seok-Hoon Jeon
Seoul Clinic of Korea Forensic Investigation, 16 Wangsan-ro, 19ma-gil, Dongdaemun-gu, Seoul 02576, Korea
Tel: +82-2-2286-1158
Fax: +82-2-928-3901
E-mail: hyuk929@naver.com

Suicide through naphthalene poisoning is rare. Prolonged hemolytic anemia and hemoglobinuria are typical symptoms of naphthalene poisoning. We report an unusual case of naphthalene poisoning. The decedent was an 87-year-old female who intentionally ingested over 5 g of naphthalene. After more than 5 hours, she was found in a drowsy state. During initial examination, hemoglobin level and urine test results were normal. Aspartate aminotransferase and alanine aminotransferase levels were elevated (854 and 1,197 U/L, respectively). Metabolic acidosis was found on arterial blood gas analysis. The patient was treated conservatively by administration of activated charcoal, calcium gluconate, insulin, and glucose. However, the patient died after 1 day of hospital admission. On autopsy, the liver showed toxic hepatitis with confluent necrosis. Naphthalene concentrations in the blood and gastric contents were 5.4 and 5.8 mg/L, respectively. In conclusion, the decedent ingested naphthalene and died due to liver failure without hemolysis.

Key Words: Toxic hepatitis; Naphthalenes; Autopsy

Introduction

Naphthalene is a bicyclic aromatic hydrocarbon ($C_{10}H_8$). Although the International Agency for Research on Cancer classifies naphthalene as a group 2B carcinogen (possibly carcinogenic to humans), it is commonly used in mothballs in developing countries [1]. Because mothballs look like candy or sugar cubes, there have been cases of accidental ingestion in children [2,3]. Moreover, suicide through naphthalene ingestion is rare. Acute symptoms of naphthalene poisoning include headaches, nausea, vomiting, diarrhea, and lethargy. Naphthalene poisoning typically induces prolonged hemolytic anemia and hemoglobinuria [4–6]. In literature, case reports of death following naphthalene poisoning are uncommon. In this case report, we describe an exceptional case of death resulting from naphthalene poisoning without hemolytic anemia.

Case Report

The decedent was an 87-year-old female who had angina, hypertension, and asthma. One year previously, she had stayed at home due to dyspnea. She had taken sleeping pills for insomnia 6 months previously and attempted suicide by ingesting eight tablets. A day

pISSN 2383-5702
eISSN 2383-5710

before she died, she did not answer the phone at 1:00 PM. It was found that she was in a drowsy state at 6:00 PM. In the emergency room, she vomited five tablets of naphthalene. After she died, two bags of naphthalene, which appeared to be purchased 10 years previously, were found in her closet. By estimating the remaining amount of naphthalene in an opened bag, she seemed to have ingested over 5 g of naphthalene.

She was afebrile with a heart rate of 102 bpm and blood pressure of 112/96 mm Hg. Her Glasgow Coma Score was 11. Initial laboratory examination results are presented in Table 1. Complete blood count was normal with hemoglobin of 14.2 g/dL, white blood cell count of 23,610 cells/mm^3, and platelet count of 358,000 cells/mm^3. Liver enzymes were elevated with aspartate aminotransferase at 854 U/L, alanine aminotransferase at 1,197 U/L, and total bilirubin at 0.78 mg/dL. Arterial blood gas analysis showed metabolic acidosis: pH 7.475, pCO_2 23.6 mm Hg, HCO_3 17.0 mm Hg, base excess −4.5 mmol/L, oxygen partial pressure (pO_2) 62.4 mm Hg, and oxygen saturation of hemoglobin (sO_2) 90.7%. Urine was yellow in color and tested negative for occult blood, leukocytes, and bilirubin. On increased cardiac markers, electrocardiogram and echocardiogram, stress induced cardiomyopathy was suspected. Hyperkalemia was found with sodium of 136 mEq/L, potassium of 6.1 mEq/L, and chloride of 100 mEq/L. Blood urea nitrogen and creatinine levels were slightly elevated. Activated charcoal was used without gastric lavage. Calcium gluconate, insulin, and glucose were used to treat hyperkalemia. Despite conservative therapy, the patient died at 6:00 AM the next day.

Table 1. Initial laboratory examination

Variable	Value
Peripheral blood	
Hemoglobin (g/dL)	14.2
WBC count (/μL)	23,610
Platelet count (/μL)	358,000
Na (mEq/L)	136
K (mEq/L)	6.1
Cl (mEq/L)	100
Osmolality (mOsm/kg)	295
AST (U/L)	854
ALT (U/L)	1197
Total bilirubin (mg/dL)	0.78
Direct bilirubin (mg/dL)	0.27
Troponin-T (ng/mL)	0.538
CK-MB (ng/mL)	5.48
Urea nitrogen (mg/dL)	29.8
Creatinine (mg/dL)	1.59
ABGA	
pH	7.475
HCO_3 (mmol/L)	17
PCO_2 (mmol/L)	23.6
O_2 saturation (%)	90.70
Urinalysis	
Glucose	Normal
Color	Yellow
Leukocyte	Negative
Occult blood	Negative

WBC, white blood cell; AST, aspartate aminotransferase; ALT, alanine transaminase; CK-MB, creatine kinase-MB; ABGA, arterial blood gas analysis.

An autopsy was performed a day after her death. In the approximately 50 mL of stomach content, four tablets of naphthalene mixed with activated charcoal were found. The concentrations of naphthalene were 5.4 and 5.8 mg/L in the blood and gastric contents, respectively. Remnant urine was low and yellow in color. The histologic finding of the liver was toxic hepatitis with zone 3 confluent necrosis and cholestasis. The confluent necrosis showed some neutrophilic infiltration without macrophage aggregates. Periportal hepatocytes were spared. Portal inflammation with predominantly lymphocytic infiltration was minimal. Fibrosis was absent (Fig. 1A–C). The right coronary artery showed severe atherosclerosis without atheroma and myocardial infarction. In the renal cortex with yellowish discoloration, autolysis without inflammatory reaction and pigment casts was confirmed (Fig. 1D).

Discussion

The acute symptoms of naphthalene ingestion include headaches, nausea, vomiting, diarrhea, and lethargy. In the liver, cytochrome P-450 metabolizes naphthalene to naphthalene 1,2-oxide. It is converted to 1-naphthol and 2-naphthol, which can be excreted though the kidney. When naphthalene is metabolized in the liver, oxidative stress induces massive hemolysis,

 https://doi.org/10.7580/kjlm.2017.41.4.137

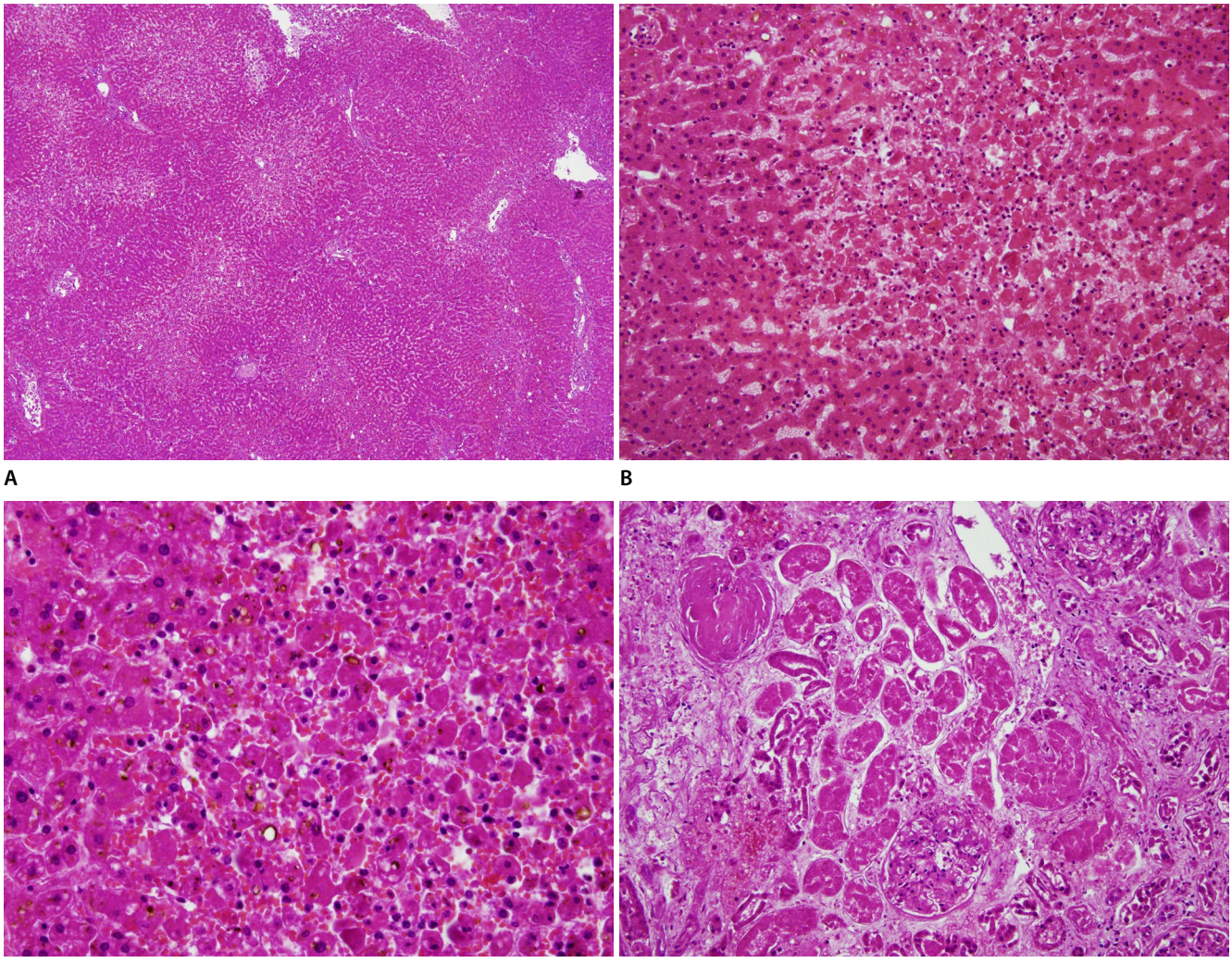

Fig. 1. Microscopic finding of liver and kidney. Liver; toxic hepatitis. (**A**) Perivenular necrosis (zone 3 necrosis) with preserved hepatocytes around portal tracts (H&E, ×40). (**B, C**) Coagulative-type necrosis of hepatocytes, cholestasis, and congestion (**B,** H&E, ×200; **C,** H&E, ×400). (**D**) Kidney: autolysis without inflammatory reaction and pigment casts (H&E, ×400).

resulting in hemolytic anemia, methemoglobinemia, hemoglobinuria, and jaundice. It is generally known that glucose-6-phosphate dehydrogenase (G6PD) deficiency increases the risk for hemolysis due to decreased glutathione stores. Hemolysis usually appears clinically at 24–48-hour post-exposure [1]. However, a case of an 18-year-old boy with hemoglobinuria occurring 16 hours after naphthalene ingestion has been reported [5]. The interval between hemolytic anemia and naphthalene ingestion can vary depending on the capacity of cytochrome P-450 in the liver, presence of G6PD deficiency, and tolerance to oxidative stress.

Per the literature, some patients who went to the hospital after naphthalene ingestion have survived through proper conservative therapy [4–6]. Therefore, death by naphthalene poisoning is uncommon. Unfortunately, the decedent had rapidly progressive naphthalene-induced toxic hepatitis presenting as fulminant hepatitis before developing hemolytic anemia and hemoglobinuria. Immediately after fulminant hepatitis, liver failure was progressing, and the patient died suddenly before developing hemolysis. In the acute phase of naphthalene poisoning, proper conservative therapy is important to save patients who have ingested naphthalene.

The lethal dose and concentration of naphthalene

is not exactly known. According to one report, the probable oral lethal dose for adults may range from 5 to 15 g [7]. However, another study found one male who survived after ingesting around 60 g of mothballs [4]. In an autopsy of a Japanese child who died by naphthalene poisoning, the blood level of naphthalene was reported at 0.55 mg/L [8]. In our case, we could not evaluate the actual uptake of naphthalene because four tablets were insoluble and five were vomited. The concentration of naphthalene in the blood (5.4 mg/L) was very high and was similar to that in gastric contents (5.8 mg/L). Because the liver's capacity for metabolism was not enough, naphthalene concentration in the blood could increase compared with that in gastric contents. If the patient died after hemoglobinuria emerged, the concentration in the blood would decrease.

The decedent who intentionally ingested naphthalene died due to liver failure before hemolytic anemia appeared. In the autopsy, toxic hepatitis without renal damage was confirmed.

Conflicts of Interest

No potential conflict of interest relevant to this article was reported.

Acknowledgments

Special thanks to Seong Ho Yoo and Baek-hui Kim for the advice and help they provided during the writing of this paper.

References

1. Hoffman RS, Howland MA, Lewin NA, et al. Goldfrank's toxicologic emergencies. 10th ed. New York: McGraw-Hill; 2015. p. 1308-11.
2. Aliyu I, Ibrahim ZF. Haemolytic anemia and mothball toxicity: a case report. Sifa Med J 2014;1:39-41.
3. Annamalai KC, Shrikirarn A, Mundkur SC, et al. Acute naphthalene toxicity presenting with metabolic acidosis: a rare complication. J Acute Dis 2012;1:75-6.
4. Tang KY. A patient presented with dark brown urine after mothballs powder ingestion. Clin Toxicol (Phila) 2017;55:674-5.
5. Chauhan V, Sharma R, Sharma K, et al. Naphthalene poisoning manifesting as hemoglobinuria. Toxicol Int 2014;21:314-5.
6. Lim HC, Poulose V, Tan HH. Acute naphthalene poisoning following the non-accidental ingestion of mothballs. Singapore Med J 2009;50:e298-301.
7. U.S. EPA. IRIS toxicological review of naphthalene (1998 Final). Washington, DC: U.S. Environmental Protection Agency; 1998.
8. Ijiri I, Shimosato K, Ohmae M, et al. A case report of death from naphthalene poisoning. Nihon Hoigaku Zasshi 1987;41:52-5.

 https://doi.org/10.7580/kjlm.2017.41.4.137