Clinical, Laboratory, Diagnostic, and Histopathologic Features of Diethylene Glycol Poisoning—Panama, 2006

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Study objective: Diethylene glycol is a toxic industrial solvent responsible for more than 13 mass poisonings since 1937. Little is known about the clinical spectrum, progression, and neurotoxic potential of diethylene glycol–associated disease because of its high mortality and the absence of detailed information in published mass poisoning reports. This incident includes the largest proportion of cases with neurotoxic signs and symptoms. We characterize the features of a diethylene glycol mass poisoning resulting from a contaminated cough syrup distributed in Panama during 2006.

Methods: This was a retrospective chart review and descriptive analysis in a tertiary level, urban health care facility. A case was a person admitted to the Social Security Metropolitan Hospital in Panama City between June 1 and October 22, 2006, with unexplained acute kidney injury and a serum creatinine level of greater than or equal to 2 mg/dL, or unexplained chronic renal failure exacerbation (>2-fold increase in baseline serum creatinine level) and history of implicated cough syrup exposure. Main outcomes and measures were demographic, clinical, laboratory, diagnostic, histopathologic, and mortality data with descriptive statistics.

Results: Forty-six patients met inclusion criteria. Twenty-four (52%) were female patients; median age was 67 years (range 25 to 91 years). Patients were admitted with acute kidney injury or a chronic renal failure exacerbation (median serum creatinine level 10.0 mg/dL) a median of 5 days after symptom onset. Forty patients (87%; 95% confidence interval [CI] 74% to 95%) had neurologic signs, including limb (n=31; 77%; 95% CI 62% to 89%) or facial motor weakness (n=27; 68%; 95% CI 51% to 81%). Electrodiagnostics in 21 patients with objective weakness demonstrated a severe sensorimotor peripheral neuropathy (n=19; 90%; 95% CI 70% to 99%). In 14 patients without initial neurologic findings, elevated cerebrospinal fluid protein concentrations without pleocytosis were observed: almost all developed overt neurologic illness (n=13; 93%; 95% CI 66% to 100%). Despite use of intensive care and hemodialysis therapies, 27 (59%) died a median of 19 days (range 2 to 50 days) after presentation.

Conclusion: A high proportion of patients with diethylene glycol poisoning developed progressive neurologic signs and symptoms in addition to acute kidney injury. Facial or limb weakness with unexplained acute kidney injury should prompt clinicians to consider diethylene glycol poisoning. Elevated cerebrospinal fluid protein concentrations without pleocytosis among diethylene glycol–exposed persons with acute kidney injury may be a predictor for progressive neurologic illness. [Ann Emerg Med. 2014;64:38-47.]

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INTRODUCTION

Diethylene glycol is a clear liquid often used as an industrial diluent. It is a potent nephrologic and neurologic toxicant in humans.[1] Ingestion of diethylene glycol may lead to acute kidney injury because of acute tubular necrosis and may also result in neurologic symptoms such as acute flaccid paralysis, cranial nerve palsies, and encephalopathy.[1] Diethylene glycol poisoning has occasionally resulted from the intentional ingestion of diethylene glycol–containing industrial products.[1] However, most cases of diethylene glycol poisoning are due to pharmaceutical products formulated with diethylene glycol as a diluent instead of a safe agent such as pharmaceutical-grade glycerine or propylene glycol. Distribution and human consumption then typically results in mass poisoning incidents.[1-18] The more recent outbreaks of diethylene glycol poisoning up until this incident have occurred more commonly in children and are associated with variable case-fatality rates, but may be as high as 98%[4,7,8,10,17,18] (Table 1).

In September 2006, an unusually large number of patients presenting with limb weakness and acute kidney injury were noted by physicians at the Social Security Metropolitan Hospital in Panama City, Panama. A subsequent international public

Editor's Capsule Summary

What is already known on this topic

The substitution of diethylene glycol for glycerin has resulted in mass pediatric poisonings characterized by fulminant acute kidney injury and death. However, little is known about diethylene glycol poisoning of adults.

What question this study addressed

The renal and neurologic findings in mass poisoning of 46 adults resulting from contaminated cough syrup.

What this study adds to our knowledge

Severe neurologic effects developed in 87% of victims, including limb or facial motor weakness, and 59% died despite use of intensive care.

How this is relevant to clinical practice

A high proportion of adult patients with diethylene glycol poisoning developed progressive neurologic effects, in addition to acute kidney injury. Facial or limb weakness with unexplained acute kidney injury should prompt clinicians to consider diethylene glycol poisoning.

health investigation identified the illness as resulting from the ingestion of a domestically produced sugarless cough syrup referred to locally as "expectorante sin azucar" ("sugarless cough syrup").[14] Extensive testing of biological and environmental samples associated with cases for multiple analytes, including metals, pesticides, glycols, and others, revealed diethylene glycol as the only possible cause (unpublished data). A nationwide assessment by the Panama Ministry of Health ultimately identified 119 cases of diethylene glycol poisoning that occurred between June 1 and October 22, 2006. Estimates of the number of citizens exposed to diethylene glycol according to product distribution records number in the tens of thousands. The true number of persons adversely affected by diethylene glycol exposure to some extent, but who remained undiagnosed, is probably higher.[14] This incident represents one of the largest outbreaks of diethylene glycol poisoning to date, to our knowledge: the first occurred in the United States during 1936, possibly affected 353 persons and killed 105 of them.[2,3]

The majority of the patients in the Panama outbreak (n=68; 57%) were hospitalized at Social Security Metropolitan Hospital. Previous published reports of similar mass poisoning incidents have described very limited clinical, laboratory, and neurologic data. The lack of data is probably because most poisonings involved children who died rapidly (within days) after exposure (likely because of a higher dose per unit body weight) and because they tend to occur in developing countries with poor access to tertiary level care capabilities and more pressing public health problems precluding detailed study of survivors.[5-13,17,18] In contrast, the majority of patients in this incident were adults (who likely received a lower dose per unit body weight compared with that of past outbreaks) and survived for several days after exposure. This enabled close observation and documentation of the clinical course of poisoning. Although diethylene glycol–associated acute kidney injury and mortality are well

Table 1. Select epidemiologic features of past medication-associated diethylene glycol mass poisonings.

Outbreak Year	Outbreak Country	Implicated Medication, Route of Exposure	Estimated Number of Persons Likely Exposed to DEG	Reported Number of Possible DEG Poisoning Cases	Reported Number of Possible DEG Poisoning Deaths	Detailed Information on Signs and Symptoms of Neurotoxicity Available	Reference
1937	USA	Elixir of Sulfanilamide, oral	353	260	105	No	2, 3
1969	South Africa	Sedative, oral	Not reported	Not reported	7	No	4
1986	India	Glycerin, route not reported but likely intravenous	Not reported	14	14	No	5
1987	Spain	Topical silver sulfadiazine, dermal	Not reported	5	5	No	6
1990	Nigeria	Acetaminophen, oral	Not reported	47	47	No	7
1990	Bangladesh	Acetaminophen, oral	Not reported	67–339*	51–236*	No	8
1992	Argentina	Propolis syrup, oral	Not reported	29	29	No	9
1995	Haiti	Acetaminophen, oral	Not reported	87–109	85	No	10, 11
1998	India	Cough expectorant, oral	Not reported	36	33	No	12
1998	India	Acetaminophen, oral	Not reported	11	8	No	13
2006	Panama	Cough syrup, oral	Thousands	119	78	Yes (n=40)	14
2008	China	Armillarisin-A, intravenous	64	15	12	Yes (n=10)†	15, 16
2008	Nigeria	Analgesic, oral	Not reported	60	57	No	17, 18

DEG, Diethylene glycol.

*There were 339 cases of acute renal failure without an obvious other cause; however, only 67 patients could be confirmed as having ingested a DEG-containing product. Of the 236 acute renal failure patients who died, only 51 could be confirmed as having ingested a DEG-containing product.

†Although some neurotoxicity information was available in this incident, the outbreak occurred as a result of intravenous administration of a DEG-containing compound, which is atypical compared with other outbreaks.