The Journal of Emergency Medicine, Vol. 19, No. 2, pp. 165–168, 2000

0736-4679/00 $–see front matter

PII S0736-4679(00)00203-1

Selected Topics: Toxicology

DETECTION OF ISOPROPYL ALCOHOL IN A PATIENT WITH DIABETIC KETOACIDOSIS

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□ **Abstract—A 29-year-old man presented to the Emergency Department with acute mental status changes. He was unable to give a history. He was found to be in diabetic ketoacidosis, although his family reported no prior history of diabetes. A toxic exposure work-up revealed the presence of isopropyl alcohol in the patient's blood. His condition improved with treatment of the ketoacidosis, and he subsequently denied any exposure to isopropyl alcohol prior to presentation to the hospital. This case provides further support to a growing body of evidence that the detection of isopropyl alcohol may not represent an acute ingestion but, rather, a byproduct of acetone metabolism in certain disease states. © 2000 Elsevier Science Inc.**

□ **Keywords—diabetes; isopropyl alcohol; ketoacidosis**

INTRODUCTION

Diabetic ketoacidosis (DKA) is a well-known clinical entity that is commonly encountered in the Emergency Department (ED). Patients present with elevated blood glucose and high plasma concentrations of ketone bodies, specifically acetoacetate, β-hydroxy-butyrate, and acetone (ACT; 1–2). Acetoacetate and β-hydroxy-butyrate provide cells with substrates that are subsequently oxidized for energy in the citric acid cycle (3). ACT is a volatile substance that at high blood concentrations is excreted unchanged, mostly by the kidneys and lungs, and at low blood concentrations is metabolized to acetyl or formyl fragments, pyruvate, or glucose (4).

Recently, several studies have speculated that ACT may be metabolized to isopropyl alcohol (IP) by alcohol dehydrogenase in certain disease states (4–6). Nevertheless, the traditional interpretation of detectable blood levels of IP suggests an ingestion of IP (7). This creates a diagnostic dilemma when the two clinical situations, acetonemia and toxic ingestion, occur within the same individual. We report such a case of a patient with altered mental status, DKA, and possible toxic ingestion.

CASE REPORT

A 29-year-old man was brought to the ED by his family because of his acute mental status changes. The family reported that he had not been feeling well over the past 3 days, with general malaise, anorexia, and lethargy. On the morning of admission he developed an acute change in consciousness, becoming unresponsive to commands and combative, leading the family to seek medical attention. They denied a history of fever, chills, cough, dysuria, polyuria, polydipsia, polyphagia, weight loss, or abdominal pain. The patient had no history of diabetes mellitus, hyperglycemia, or any other medical, neurologic, or psychiatric condition. The family could not exclude the possibility of drug or other toxic ingestion. He was known to have a history of tobacco and alcohol

RECEIVED: 17 September, 1999; FINAL SUBMISSION RECEIVED: 15 February, 2000;
ACCEPTED: 3 April, 2000

Table 1. Routine Admission Lab

Test	Result
Plasma glucose	2090 mg/dL
Plasma potassium	6.5 mMol/L
Arterial pH	7.07
Plasma bicarbonate	12 mMol/L
Blood urea nitrogen	78 mg/dL
Creatinine	5.4 mg/dL
Plasma sodium	138 mMol/L
Plasma chloride	89 mMol/L
Plasma lactic acid	1.5 mMol/L
Plasma acetoacetate	Positive
Serum osmolality	450 mOsm/kg
Hemoglobin	16.8 G/dL
Hematocrit	56.7%

abuse, ingesting three to six drinks daily for 10 years. His last alcohol ingestion was 5 days previous to presentation because of his recent malaise.

On admission, physical examination revealed a well-nourished young man who was extremely agitated and combative. He was afebrile, and vital signs were within normal limits with the exception of a heart rate of 112 beats/min. He did not follow commands, answered no questions, and made incomprehensible sounds. He localized to painful stimuli and displayed an intermittent disconjugate gaze, but had no signs of upper or lower motor neuron damage. The Glascow Coma Score was 11. The remainder of the physical examination was unremarkable with the exception of markedly poor skin turgor, extremely dry mucous membranes with scattered denuded tissue, and the breath had an ACT odor. It was felt at the time that these findings were consistent with either toxic ingestion or severe dehydration.

The results of a routine admission laboratory work-up demonstrated an extremely high plasma glucose with evidence of acidosis (Table 1). Blood, urine, and sputum cultures were eventually found to be negative. Computed tomography (CT) scan of the head was performed and was negative. A high serum osmolality, an elevated osmol gap of 30, and the metabolic acidosis subsequently prompted a toxic ingestion work-up. The toxicology laboratory screen detected a small amount of IP along with the expected elevated ACT level (Table 2). Shortly after admission, the patient's mental status further deteriorated, and he was intubated for airway protection. He was subsequently transferred to the Intensive Care Unit for further monitoring and treatment of DKA. The Toxicology service was consulted to evaluate the patient and make recommendations for treatment.

Upon initial evaluation, the Toxicology service promptly recognized the possibility that the positive IP screen could be due to a shunting mechanism in the degradation pathway of ACT (see Discussion). They recommended determination of another IP level after the patient's DKA began to resolve. The second IP level was not detectable. During the remaining hospital course, the patient's DKA resolved, his mental status returned to normal, and he was extubated. After extubation he was able to assure us with complete certainty that he had not ingested any substances prior to presentation to the ED. His diabetes has persisted and is currently managed with an appropriate regimen of insulin. He has had no further episodes of DKA.

DISCUSSION

Altered mental status is a common patient presentation in the ED. Often the etiology is not clear, and the most emergent situations have to be considered and excluded promptly. This is a case in which several pathologic processes could have been involved. The patient could not give a history, which is often the case in the ED, thus compromising the accuracy of the events prior to presentation. There was no history of diabetes mellitus, and there appeared to be a toxic ingestion. This particular situation presented a diagnostic dilemma and, therefore, each process in the differential diagnosis, especially toxic exposure, needed to be explored and excluded.

IP is a clear, colorless liquid that is readily found in various disinfectants, toiletries, paint removers, antifreeze, and as a 70% rubbing alcohol solution. Absorption occurs rapidly via oral exposure, but transdermal, rectal, and inhalational routes can also result in significant absorption. Metabolism is carried out by alcohol dehydrogenase in a concentration-dependent manner. Eighty percent of IP is metabolized to ACT, and the remainder is excreted unchanged in the urine and via the lungs (Figure 1). ACT is subsequently excreted by the

Table 2. Admission Toxicology Lab

Blood or Urine Test	Result
Isopropyl Alcohol (b)*	5 mg/dL
Acetone (b)	97 mg/dL
Methanol (b)	0 mg/dL
Ethylene glycol (b)	0 mg/dL
Ethanol (b)	0 mg/dL
Salicylate (b)	5 mg/dL
Acetaminophen (b)	<5 mg/dL
Barbiturate (u)†	negative
Benzodiazepine (u)	negative
Opiate (u)	negative
Cannabis (u)	negative
PCP (u)	negative
Cocaine (u)	negative
Amphetamine (u)	negative

* b = blood.
† u = urine.

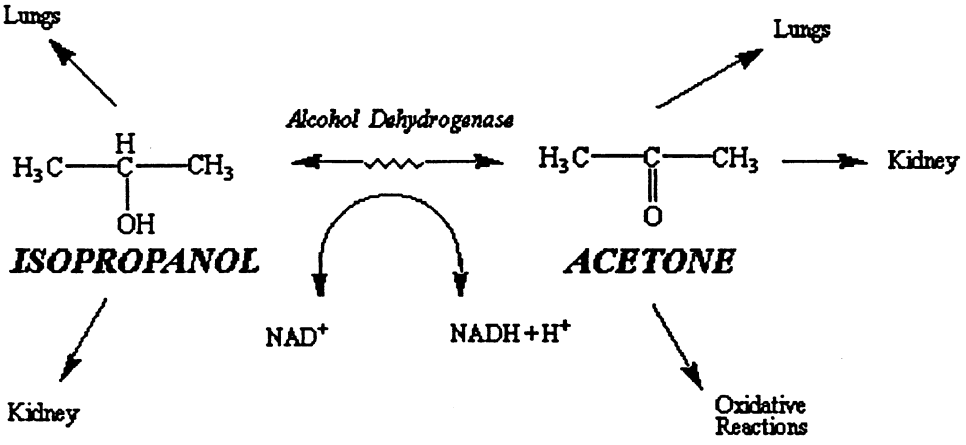

Figure 1. Acetone metabolism. Acetone is converted to isopropyl alcohol via alcohol dehydrogenase. NAD = nicotinamide adenine dinucleotide, NADH = reduced form of NAD.

kidneys and lungs or metabolized to products that enter the gluconeogenic pathway (4,8–9).

Clinical findings associated with IP intoxication include central nervous system depression, weakness, lethargy, ataxia, odor of ACT, apnea, and hypotension. Laboratory findings include ketonemia; increased osmolality; euglycemia; and usually, no evidence of metabolic acidosis. Treatment of patients with IP ingestion is, for the most part, supportive, particularly the cardiac and pulmonary systems. Some feel that in extreme overdoses or in severely ill patients, hemodialysis is indicated (9).

Traditionally, detectable levels of IP in humans has been considered indicative of exposure to the agent (7). Recently, several investigators have made new observations to challenge this theory. After detecting IP in the blood of acetonemic cows, Robertson et al. speculated that ACT could be converted to IP (10). Lewis et al. and Davis et al. reported finding IP and ACT in the blood of autopsy patients not previously exposed to IP (4,6). Lewis demonstrated the production of IP in rats treated with ACT, and Davis demonstrated in vitro production of IP from ACT. Jones and Andersson reported detecting IP and ACT in a motorist with hyperglycemic ketoacidosis and alcoholic (starvation) ketosis (11). Furthermore, Bailey reported detecting IP in the blood of five hospitalized acetonemic type 1 diabetics (5).

The shunting mechanism by which the biotransformation of ACT to IP occurs can be explained in several steps (Figure 1). When glucose is unavailable as an energy source, as in uncontrolled diabetes, fatty acid oxidation is used to provide substrates for energy production. This oxidation generates reduced nicotinamide adenine dinucleotide (NADH) that can in turn reduce ACT to IP in the presence of high levels of ACT. The oxidized product of NADH, NAD, can then be reused for fatty acid oxidation, leading to further ketone body and NADH production. Therefore, a high NADH/NAD (redox) ratio would favor the production of IP from ACT (4,6). Disease states known to have these increased redox states include diabetes mellitus and chronic alcoholism (6,12). It is proposed that metabolism is shifted toward the production IP from ACT only in those patients with extremely high levels of ACT from massive hyperglycemia coupled with a state of induced alcohol dehydrogenase as is seen with chronic alcohol ingestion (4).

Our patient had a complicated clinical picture on presentation. He had several clinical findings classic for DKA, including anion gap metabolic acidosis, increased serum potassium, dehydration, ketonemia, and mental status changes; however, there was no history of diabetes mellitus. He also had several clinical findings consistent with IP ingestion, including mental status depression, increased osmolality, and ketonemia. Although we postulated two disease processes, DKA and IP ingestion, it is more likely that the situation represented biotransformation of ACT to IP rather than acute IP ingestion. It is our intention to make others aware of this possibility when interpreting similar clinical situations.

This case supports previous reports of endogenous biotransformation of ACT to IP in certain disease states. Of special interest in this case was the fact that a history of toxic exposure to IP at first could not be confirmed or denied. Our detection of IP in this patient's blood traditionally would have been interpreted as a toxic exposure to the agent. However, as previously noted, new evidence has emerged that makes it necessary to consider several pathologic processes when interpreting detectable levels of IP in the blood. We suggest that the information provided herein be considered by emergency physicians when IP is detected in diabetics and chronic

alcoholics and suggest that these observations may be a starting point for further studies related to toxic co-ingestion.

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