

# A “glue sniffer” teenager with anuric renal failure and hepatitis

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“Inhalant abuse” is a common form of volatile drug abuse throughout the world especially in developing countries. This substance mainly contains toluene. Acute toluene inhalation produces a biphasic response with an initial central nervous system (CNS) excitation followed by CNS depression as well as various metabolic alterations. Chronic inhalational abuse is associated with muscular weakness, gastrointestinal symptoms, renal and hepatic injury. In this report, a 16-year-old boy presented with jaundice, nausea, vomiting and reduced urine output. He developed severe acute renal/hepatic damage due to abuse of gas products. Since toluene is the main toxic agent involved in glue sniffing which is metabolized to hippuric acid, the present case was treated with continuous hemodiafiltration, plasma exchange and conservative therapy to eliminate hippuric acid. The jaundice gradually disappeared, he had complete recovery of renal/hepatic functions in ten days. We aimed to increase the awareness among emergency physicians that “glue sniffing” should be considered in the differential diagnosis of unexplained reversible acute renal/hepatic damage.

**Key words:** glue sniffing, hepatitis, acute kidney injury, jaundice.

Toluene is the main toxic agent involved in glue sniffing and the most widely abused inhaled volatile drug. It produces a biphasic response: the first stage is often described as euphoria, followed by excitability, disinhibition, impulsive behavior and the second stage is characterized by central nervous system (CNS) depression.<sup>1</sup> It can also lead to cardiac arrhythmias, syncope, glomerulopathy, respiratory failure, bone demineralization and sudden sniffing death syndrome.<sup>2-4</sup>

Acute kidney injury and hepatitis with cholestasis has rarely been attributed to toluene abuse.<sup>5,6</sup> The present case shows that “inhalant abuse” may cause serious organ dysfunction and describes the elimination of the substance from the patient.

## Case Report

A 16-year-old boy presented to the emergency department with a history of nausea, vomiting,

jaundice and reduced urine output for three days. There was no history of previous illness. He had begun to practice “glue sniffing” eight months ago and he increased the amount of inhalant in the last two months. He had sniffed approximately 50 ml/day (one tube) of adhesive during the previous two days before his admission to hospital. Upon arrival to the emergency department, he was drowsy with Glasgow coma scale (GCS) 13, mildly dehydrated, his pulse and blood pressure were 90/min and 124/79 mm Hg, respectively. He also had yellowish staining of the sclera and conjunctival hyperemia. There were no palpable intra-abdominal masses or hepatosplenomegaly. Examination of other systems were unremarkable.

Laboratory assessment revealed: hemoglobin 13.9 g/dl, white blood count, 19,000/mm<sup>3</sup> with predominant polymorphs (86.2%) and

platelet count 214,000/mm<sup>3</sup>; Serum creatinine 9.6 mg/dl, urea 178 mg/dl, potassium 3.6 mEq/L, sodium 131.7 mEq/L and chloride 93 mEq/L. Venous blood gas analysis showed pH of 7.45, PCO<sub>2</sub> of 30.2 mmHg, HCO<sub>3</sub> of 20.8 mmol/L and PO<sub>2</sub> of 49.2 mmHg. Other laboratory findings were as follows: aspartate aminotransferase (AST) 778 U/L, alanine aminotransferase (ALT) 1681 U/L, total bilirubin 4.3 mg/dl, direct bilirubin 2.92 mg/dl, international normalized ratio (INR) 2.07, gama glutamyltransferase (GGT) 89 U/L, alkaline phosphatase (ALP) 223 U/L, total protein 6.1 g/dl, albumin 3.6 g/dl, calcium 8.8 mg/dl, phosphorus 4.6 mg/dl, uric acid 8.1 mg/dl and serum paracetamol <2.5 µg/ml. Urine analysis showed pH of 6.5, protein negative with no leukocyte or red blood cells.

Abdominal ultrasound showed increased renal parenchymal echogenicity in (grade II) both kidneys with normal size; liver was normal in size and parenchymal echogenicity. There was no feature of obstructive uropathy. Chest X-ray and electrocardiography (ECG) were normal. Patient's mental status improved within few hours; neuroimaging was not obtained.

The patient was admitted to the pediatric intensive care unit (PICU) due to renal, hepatic damage and encephalopathy. Since acute renal and hepatic damage secondary to toxic agent ingestion such as drugs, mushrooms and wild plants either intended or unintended constitutes 20-40% of the cases and is more common in adolescents in our country; these group should have been ruled out upon presentation. Due to these toxic agents plasma exchange with plasma was administered as

a first step of management. At the second day of his admission the management plan was substituted to continuous venovenous hemodiafiltration (HDF) since the patient was awake and he stated that he is a glue sniffer which involved mainly toluene. M-60 dialyser type was preferred, dialisan Dp-4 solution was used, and 3600 ml ultrafiltrate was taken from the patient within 48 hours.

At 24 hours, he developed hypertension (200/90 mmHg); enalapril, amlodipine and esmolol were administered. Esmolol was ceased at the second day of his admission since his blood pressure level (160/80 mmHg) gradually decreased. He had been anuric since admission until the fourth day. After the first urine output fractional excretion of sodium was calculated as 2.6 %. Urine output, urea and creatinine levels are shown in Figure 1. By day seven, the blood pressure, the blood urea and serum creatinine levels were within normal limits with normal urine output (Fig. 1). Due to evidence of coagulopathy and increased INR, fresh frozen plasma was administered to the patient during hospitalization. At tenth day of admission the jaundice gradually disappeared and hepatic functions returned to normal (Fig. 2). The patient is under the care of psychiatrist for psychotherapy. Informed consent was obtained to publish this case report.

**Discussion**

Toluene is the main toxic agent involved in glue sniffing. Glue sniffing and other forms of solvent abuse are becoming increasingly common in adolescents especially in developing countries due to several factors such as easily

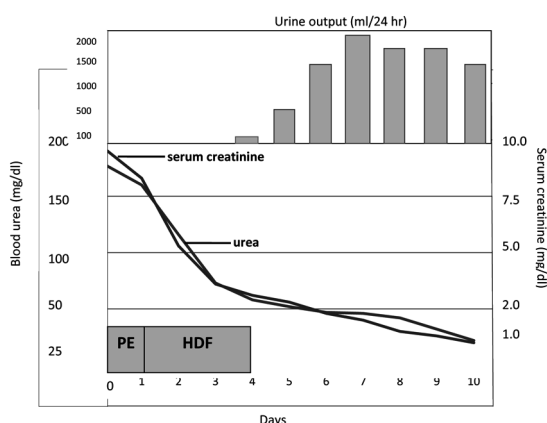


Fig. 1. Renal function tests (HDF:hemodiafiltration)

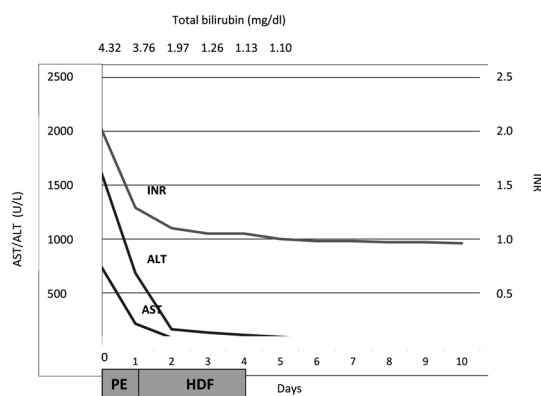


Fig. 2. Hepatic function tests (PE: plasma exchange; INR: international normalized ratio)

accessible, inexpensive and legal to buy.<sup>7</sup>The prevalence of inhalant use in adolescents in Turkey is about 4%.<sup>8</sup>

As a volatile hydrocarbon toluene, which is highly lipid soluble when inhaled, is absorbed by the lungs and binds to lipoproteins and rapidly diffuse throughout the body and into the CNS. The lethal dose for toluene via inhalation is over 10000 ppm (pints per milliliter).<sup>9</sup>The majority of toluene (70–80%) is metabolized in hepatic microsomes by oxidation to benzoic acid, which is conjugated with glycine to form hippuric acid and excreted in urine with half-life of 2-3 h.<sup>9,10</sup> Urinary concentrations of up to 1.5-1.6 g hippuric acid per g of creatinine are considered normal. When higher levels are detected, exposure to toluene is assumed. Exposure is considered excessive when hippuric acid levels in the urine are higher than 2.5 g per g of creatinine.<sup>10</sup>

Gastrointestinal symptoms are the most common complaints and most patients presents with nausea and vomiting.<sup>6</sup> The present case had a history of nausea, vomiting, jaundice and reduced urine output for three days. These findings were also supported by previous reports.<sup>1,5,6</sup>

In our patient, initial altered mental status can be explained by the second phase of solvent encephalopathy.<sup>11</sup>Previous reports showed that acute inhalation produces a biphasic response with an initial CNS excitation followed by CNS depression.<sup>11,12</sup> We believe that the first stage, in our case which is thought to be euphoria, happened before admission.

Although the toxic effects of toluene mainly occur on urinary system serum creatinine increases in nearly 20% of patients.<sup>12</sup> Wide spectrum of renal diseases may develop in association with toluene inhalation. They include rhabdomyolysis, distal renal tubular acidosis, and anti-glomerular basement membrane antibody mediated glomerulonephritis.<sup>6,13</sup> Nephrotoxic injury occurs due to toluene and its metabolite hippuric acid which leads to distal renal tubular acidosis by inducing permeability changes in the nephron leading to backward leakage of secreted acids. Acid retention causes calcium mobilization, hypercalciuria and renal calculi.<sup>9,14</sup> Since our patient had severe renal toxicity (creatinine 9.6 mg/dl) as well as hepatic damage, HDF was instituted for the

suspicion of toluene poisoning. HDF has some crucial features which makes it useful in pediatric population. In case of severe toluene toxicity HDF should be preferred as a first line treatment modality because it has a safe technique, allows controlled ultrafiltration (continue administration), and eliminate the toxic metabolites (smaller dialysis filters) better than hemodialysis and plasma exchange.<sup>3,14</sup>

Toluene abuse has been associated with liver damage and the associated increase in transaminases and ALP.<sup>5,6</sup> The hepatotoxic potential of toluene inhalation has been reported in animals as well as human studies. Animal studies showed that toluene leads to oxidative injury in the liver and induces elevation of serum bile acids.<sup>15</sup> In 1971, O'Brien et al.<sup>5</sup> reported a case of a glue sniffer who was admitted with severe hepatorenal toxicity and persisted with elevated ALP levels after 7 days of supportive treatment and this was consistent with previous reports. Differently, it was reported that ALP was not elevated and GGT was only mildly elevated in patients who died.<sup>12</sup> In our patient although ALP and GGT levels were normal; both jaundice, which is a sign of hepatobiliary injury, and elevated transaminases were the evidences of hepatotoxicity.

Weakness was a prominent symptom in the largest case series with 22 patients which was reported by Cámara-Lemarroy et al.<sup>6</sup> and they found that all patients presented with some degree of weakness, ranging from mild muscular weakness in the extremities to full paralysis in two cases. Since in our case serum potassium was 3.6 mEq/L and he had no complaint of weakness, we believe that this supports the opinion that weakness is closely associated with hypokalemia.

Although glue sniffing can cause life-threatening toxicity to various other systems of the body, in our case mild encephalopathy, hepatobiliary and renal toxicity occurred. In the literature cerebral infarction, aplastic anemia and even sudden death secondary to toluene sniffing have been reported.<sup>15-17</sup> Chronic inhalational toluene abuse is associated with muscular weakness, gastrointestinal symptoms (pain, nausea, vomiting), renal tubular acidosis (hypokalemia and metabolic acidosis), hepatic injury and neuropsychiatric

symptoms. Patients with long-term inhalational abuse may develop progressive irreversible encephalopathy with cognitive difficulty and cerebellar ataxia. Abnormal magnetic resonance imaging findings including; generalized cerebral, cerebellar, and brainstem atrophy; atrophy of the corpus callosum; loss of gray-white matter discrimination; multifocal high signal intensity in the cerebral white matter; and hypointensity of the thalami.<sup>1</sup> Significant inhalational exposure causes an easily recognized odor to the breath that may persist for several days after exposure ceases.<sup>1,7</sup>

Toluene inhalation is one of the most common forms of drug abuse in Turkey that carries various health-related risks.<sup>2-4,7,8</sup> The acute CNS symptoms are accompanied by some metabolic alterations as well as organ damage and dysfunction. Although gastrointestinal complaints are common and most patients presented with nausea and vomiting they are not specific.

The first limitation of this report was demonstrating the increased concentration of toluene in the biological samples and the increased concentration of hippurate in the urine on presentation. The second limitation was the absence of neuroimaging.

The aim of reporting this case is to emphasize that glue sniffing should be included in the differential diagnosis of any teen patient presenting with unexplained acute renal/hepatic failure especially in patients who do not have any environmental exposure.

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