

# A Challenge between Central Nervous System Infection and Lead Toxicity: Opioid Case Reports from Iran

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## Abstract

Although lead pollution has long been known as a cause of poisoning, it has remained a challenge to reliably diagnose it due to its common symptoms in various diseases. In this article, we report two cases of acute loss of consciousness due to the ingestion of opium-contaminated with lead. The reported cases share patterns of symptoms similar to meningitis and encephalitis which are usual etiology for the loss of consciousness. Lead poisoning is not a usual etiology for loss of consciousness and is considered in cases of occupational or environmental exposure. These reported cases showed a pattern similar to meningitis and encephalitis, but due to the unusual manifestations during their admission and coexistence with gastrointestinal symptoms, we were led to consider poisoning as the cause of consciousness loss. Lead poisoning often goes unrecognized due to a low index of suspicion, but it may turn out to be fatal. Therefore, it should be considered in the differential diagnosis of any neurobehavioral deficits in substance abusers.

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## What's Known

- Several cases of CNS involvement due to acute lead poisoning have been reported to date, but in none of them, CNS infections have been evaluated while these infections have appreciable mortality rate. Also, there appears to be no research investigating a topic similar to what we did in our study.

## What's New

- Lead poisoning is not a usual etiology for the loss of consciousness, especially in adults, and it may prove to be fatal. Also, this poisoning shares patterns of symptoms similar to meningitis and encephalitis as occurred in our cases, so we recommend considering lead toxicity in the differential diagnosis of any neurobehavioral deficits in substance abusers.

## Introduction

Both Lead toxicity and central nervous system (CNS) infection may be presented with loss of consciousness,<sup>1</sup> but it seems the former, which could turn out to be a fatal toxicity, is underestimated for two reasons: It is an unusual etiology for the loss of consciousness;<sup>2</sup> second, it could be mistaken for meningitis and encephalitis because of similar clinical presentation and cerebrospinal fluid (CSF) changes.<sup>1,3</sup>

Lead is a potent occupational and environmental toxin. Human exposure to it occurs through various sources including industrial processes. These exposures have been decreased because of increased public health awareness and governmental rules.<sup>4,5</sup> Iran has a high rate of substance abuse. Opium consumption is a common form.<sup>2</sup> The contamination of opium with lead is a new source of lead toxicity in Iran.<sup>6,7</sup> The main goal of contamination of illegal substances is to increase the weight for more profit.<sup>7</sup> Up to now, similar cases have not been reported because toxicologists and infectious specialists have managed to diagnose the source of their patients' loss of consciousness based on references that have been reported in countries with a different epidemiology

of addiction from Iran. As mentioned above, in Iran, there is a special source of lead and the approach to loss of consciousness should be indigenized.

Here, we report two cases of lead poisoning that had similarities with meningitis and encephalitis. The authors hope the report of such cases bear some insights for the clinicians.

## Case Presentation

### Case 1

Between August 2017 and September 2017 in Tehran, a 59-year-old man was brought in the Emergency Department with fever, disorientation, and agitation which had developed over the previous two days. He had also suffered from a three-month period of nausea and abdominal pain along with a progressive weight loss of 17 kg. He had used opium every day for 20 years. His current medication included omeprazole 20 mg daily and ondansetron 4 mg bid.

On physical examination, the patient was agitated and disoriented. He had an axillary temperature of 37.4 °C, blood pressure of 110/70 mmHg, pulse of 100 per minute, and a respiratory rate of 18 per minute. He looked pale. Neurologically, he was awake but disoriented. No other abnormalities were found.

Laboratory tests showed an elevated urea (50 mg/dl), creatinine (1.7 mg/dl), sodium (153 mmol/L), and leukocytosis of 13000 per mm<sup>3</sup> with a shift to left (75% neutrophil, 20% lymphocyte, and 5% mixed cells), a low hemoglobin of 10.3 mg/dl with a mild hypochromic microcytic smear; evaluation for hemolysis was negative. Other metabolic evaluations including glucose were normal. Serum drug screening revealed a positive level for opiates. The brain computerized tomography (CT) scan, electroencephalography (EEG), and his cerebrospinal fluid (CSF) analysis were normal. As we could not rule out herpetic encephalitis with these data, he was commenced on intravenous acyclovir 750 mg every 12 hours and subcutaneously methadone 5 mg every 12 hours to control opioid withdrawal syndrome as well as providing electrolyte correction. After two days, his consciousness had not changed. Repeated evaluation of CNS, including brain Magnetic resonance imaging (MRI) and CSF analysis, showed normal results.

To further the evaluation of his abdominal pain, the abdominal ultrasound and CT scan were requested which revealed a coarse echo of the liver and a diameter of the portal vein of 13 mm. The upper and lower endoscopy showed gastritis and internal hemorrhoid. The Magnetic

resonance cholangiopancreatography (MRCP) was normal. On the third day of admission, he had experienced a tonic-clonic seizure. EEG showed evidence of encephalopathy, but his brain CT scan remained normal. On the fourth day of admission, his gastric secretion changed to coffee-ground appearance. Finally, he had a cardio-pulmonary arrest and passed away. After his death, we received a negative result of his CSF herpes virus (HSV) polymerase chain reaction (PCR), and his serum lead level showed 98 µg/dl.

### Case 2

Between August 2017 and September 2017 in Tehran, a 60-year-old man was brought in the Emergency Department with a three-day history of agitation and lethargy. He also had a tonic-clonic seizure and upward gaze on admission. He had used opium for 20 years. He had cholecystectomy 15 years ago. On physical examination, the vital signs showed a fever of 38 °C (axillary) and a tachycardia of 110 per minute but normal blood pressure and respiratory rate. Neurologically, he was lethargic and disoriented. No other abnormalities were found.

Laboratory tests showed an elevated urea (42 mg/dl), lower normal limit of hemoglobin (11.4 mg/dl), but normal liver function test and serum glucose. Serum drug screening revealed a positive level for opiates. His brain CT scan was normal, but CSF analysis detected pleocytosis of 15 with 80% polymorphonuclear cells and 20% lymphocyte, glucose 104, and a high protein of 89 mg/dl. The EEG showed mild diffused encephalopathy with a generalized seizure. He was commenced on ceftriaxone (2 gr bid i.v.), ampicillin (2 gr i.v. q4h), vancomycin (1 gr bid i.v.), and acyclovir (600 mg tds i.v.) empirically along with phenytoin (100 mg tds i.v.) and methadone (5 mg bid s.c). When the results of his CSF HSV PCR test, gram stain and culture, and blood cultures were available and negative, all antibiotics and acyclovir were held. Due to his blood lead level of 128 µg/dl, penicillamine (250 mg qid via nasogastric tube) was administered to him. Regrettably, his condition deteriorated as his conscious level decreased and he experienced tachypnea and dyspnea for which supportive respiratory care was provided. Also, D-penicillamine was discontinued and Ethylene diamine tetra acetic acid (EDTA) (750 mg tds) and British anti-Lewisite (BAL) (200 mg q 4h) were administered. On the sixth day of his admission, he experienced cardiac arrest and died.

Written informed consents from the patients' next of kin were obtained for reporting the cases.

## Discussion

In our cases, different evaluations including lumbar puncture were done and the patients were admitted with suspected diagnoses of acute meningitis and encephalitis. Given the high mortality rate of bacterial meningitis and herpetic encephalitis, the patients were empirically treated for them. After three days of unresponsiveness, another diagnosis (lead toxicity) was performed due to the negative reevaluation and unrelated events to mentioned CNS infections such as abdominal pain, weight loss, and gastrointestinal bleeding without other signs of severe sepsis.

Unfortunately, lead toxicity has nonspecific symptoms and signs and similarities to meningitis and encephalitis. CNS symptoms can appear immediately after exposure or may be delayed for several months/years and may be manifested by the loss of memory, loss of vision, cognitive and behavioral problems, and brain damage/mental retardation.<sup>1</sup> Also, CSF analysis could be similar to CNS infections mentioned above. Lead exposure reduces the tightness and augments the permeability of tight blood–CSF barrier; then, CSF analysis may show mild changes including pleocytosis and high protein.<sup>3</sup> Both the CNS infections mentioned earlier and lead toxicity have high morbidity and mortality rates and neither should be misdiagnosed.<sup>1, 8, 9</sup>

In 2006-2008, similar articles were published about the adulteration of opium with lead which in one of them, Aghaee Afshar and colleagues recommended routine screening of lead toxicity in opium users.<sup>4</sup>

Jalili M and colleagues reported a chronic lead toxicity in a patient with abdominal pain which had bought opium from the black market, from the same source for many years. They concluded that metabolic diseases such as lead toxicity should be in differential diagnoses (DDx) of abdominal pain.<sup>10</sup>

Hayatbakhsh and colleagues evaluated 249 opium users with GI symptoms and signs of lead toxicity. They concluded that this toxicity in opium addicts was an increasing problem in Iran and lead toxicity should be in DDx of abdominal pain.<sup>6</sup>

Ghane and colleagues collected data from the largest toxicology center in Iran to explain the epidemiology of an outbreak of lead toxicity in opium addicts. Over 7 months, 4294 poison cases were reported, of which the lead level was checked only for 80 patients because of the constraints. They had been presented with gastrointestinal symptoms and signs. Their study emphasizes the consideration of lead adulterated opium and heroin as a major risk and

the need for a closer monitoring of illicit drugs.<sup>2</sup>

Soltaninejad and Shahin Shadnia reviewed 18 articles about 324 case reports of lead toxicity in opium users. Some cases had neurological symptoms (peripheral or central); two of them had been presented with loss of consciousness. They concluded lead toxicity depended on route, amount and duration of opium abuse, and that public health experts should monitor the evaluation of the risk of this poisoning in opium users.<sup>7</sup>

There was an agreement on lead poisoning as a challenging issue because of similarities in symptoms and signs and having an unusual source. But in none of the previous articles, the loss of consciousness was evaluated for meningitis and encephalitis while these infections and lead toxicity are two important DDx in these patients and missing each of them is a big mistake that could result in morbidity and mortality.<sup>8, 9</sup>

In original references, lead toxicity has not been included in usual DDx of loss of consciousness.<sup>11-13</sup> Lead toxicity in opium users should be among routine DDx of loss of consciousness in countries in which illicit drugs are contaminated with lead. In addition, an Iranian loss of consciousness guideline should be written.

Also, by presenting these cases in toxicology centers, the need for the evaluation of mentioned CNS infections (meningitis and encephalitis) in loss of consciousness patients will be emphasized.

## Conclusion

The greatest danger in the emergent management of lead toxicity is the failure to recognize the possibility of lead poisoning. This is not uncommon because the symptoms and signs of lead toxicity, including neurologic manifestations, are subtle or similar to CNS infections and could be easily overlooked. Therefore, all patients with the loss of consciousness and opium addiction should be evaluated for lead toxicity in addition to routine etiologies for the loss of consciousness.

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**Conflict of Interest:** None declared.

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