CASE REPORT

Delayed hypoxic encephalopathy: a rare complication of methadone poisoning in two cases

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Abstract

Methadone is a kind of opioid that is used to reduce the pain of addicts who decide to withdraw drugs. Sometimes due to a lack of appropriate cautions, this drug will be accessible to children, and poisoning might occur. Methadone poisoning usually presents with the loss of consciousness and pinpoint pupils. Herein, we present two cases of delayed hypoxic encephalopathy that had been poisoned by methadone.

Case Presentation

The first case was a 4-year-old female patient who firstly presented with nausea and vomiting; then, the case was discharged; however, 1 week later, the case was returned with the loss of consciousness and poisoning by methadone confirmed in her urine. Again 2 weeks later, the case returned to the hospital, developing weakness of limbs, slurred speech, and abnormal movement of her limbs. The second case was an 11-year-old female patient who was admitted to an intensive care unit due to the loss of consciousness and methadone poisoning. After providing supporting care, she was discharged but returned to the hospital 5 days later. She developed weakness of limbs, abnormal movement of tongue and extremities, and slurred speech. In their last admission, the magnetic resonance imaging of the patients revealed hypoxic damage in the basal ganglia; therefore, delayed hypoxic encephalopathy was confirmed.

Conclusion

Patients with methadone poisoning should be observed for at least 1 and a half months after poisoning. Moreover, parents should notice that in the case of observing abnormal neurologic manifestations bring their child as soon as possible to a hospital to prevent irreversible

damage to the brain.
Keywords: Methadone Poisoning; Delayed Hypoxic Encephalopathy; Neurology
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Introduction

Methadone is a kind of opioid that is used to reduce the pain of addicts who decide to withdraw drugs. Drug abuse gradually makes some metabolic changes in the brain; methadone is administrated to reverse these metabolic changes (1, 2). As parents who are addicted to drugs are prevalent in the community, and some of these parents do not put these drugs in safe places, children could be easily poisoned by methadone (3). Methadone poisoning typically presents acutely with the loss of consciousness, respiratory depression, and miotic pupils (4, 5). Herein, we present two cases of delayed hypoxic encephalopathy as a rare complication of methadone poisoning.

Case Presentation

Case 1

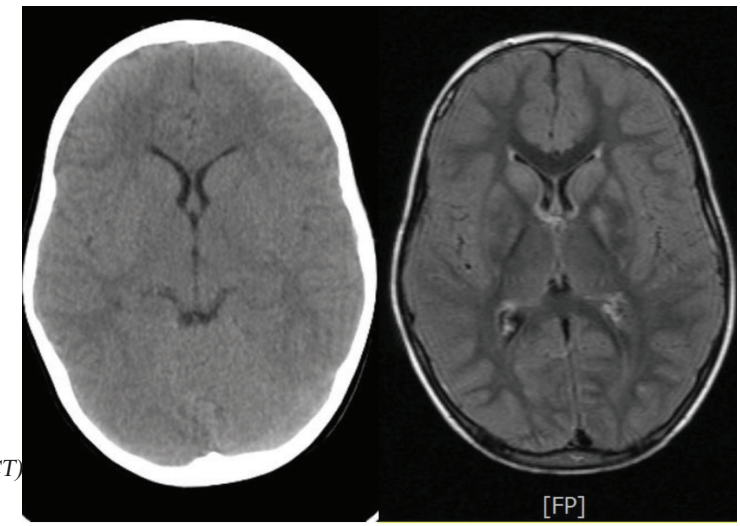
The patient was a healthy 4-year-old female patient manifesting nausea, vomiting, and cough. Anti-nausea drugs were prescribed for her, and the episodes of nausea and vomiting stopped. After a week, nausea, vomiting, and cough persisted, and she developed high blood sugar, loss of consciousness, staring for more than 30 seconds, and pinpoint pupils; therefore, the case was transferred to the emergency room (ER). The brain computed tomography scan was normal; however, methadone was observed in her urine by taxonomic test, and drug abuse was confirmed; accordingly, naloxone was prescribed. After reaching a well status and becoming well, the patient was discharged 8 days after admission. Two weeks after discharge, she returned to the ER again, developing weakness in both upper and lower extremities, slurred speech, and abnormal movement of limbs. Her physical examinations revealed weakness in limbs, aphasia, chorea, upward plantar reflex, and an increase in deep tendon reflexes. The laboratory data of the case included hemoglobin (Hb) of 10.7, white blood cell (WBC) of 10.6 with dominancy of neutrophil, platelet count of 540, erythrocyte sedimentation rate (ESR) of 22, blood urea nitrogen (BUN) of 18, sodium (Na) of 141, potassium (K) of 4.5, glucose of 81, C-reactive protein (CRP) of 10, negative results for blood culture, and normal cerebrospinal fluid evaluation. Magnetic resonance imaging (MRI) in the second admission of the patient revealed ischemia and damage in both her basal ganglia (Figures 1 and 2).

Case 2

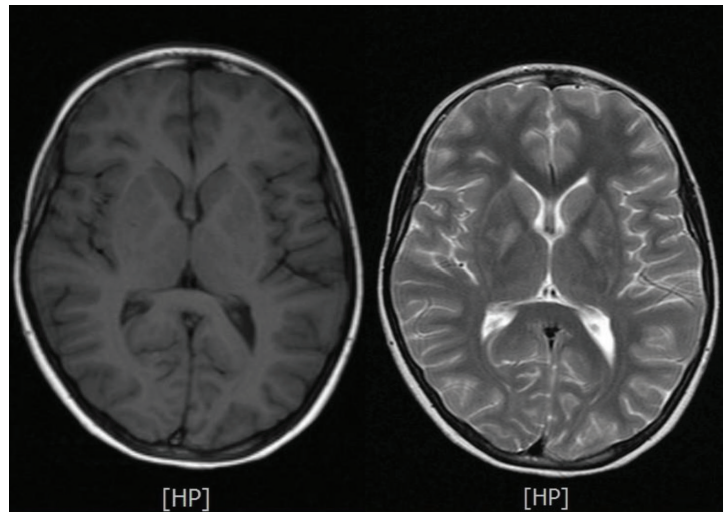
The patient was a healthy 11-year-old case who was admitted, for the first time, to an intensive care unit due to the loss of consciousness, pinpoint pupils, and methadone poisoning confirmed by urine toxicology. After administering naloxone and performing supportive care, she was transferred to the neurology ward. The case could talk fluently, walk normally, and had normal neurologic manifestation. Her brain MRI was normal; therefore, she was discharged from the hospital 3 days after admission. After 5 days,

she returned to the hospital with an abnormal movement of the tongue and inability to swallow and gradually developed the abnormal movement of her extremities, weakness, slurred speech, and inability to sit and walk. The laboratory data of the case included Hb of 11.1, WBC of 10.5 with dominancy of neutrophil, platelet count of 490, ESR of 20, BUN of 15, Na of 144, K of 4.3, glucose of 85, and CRP of 9. The lumbar puncture of the patient revealed no significant finding. The MRI of the patient revealed ischemic damage to the basal ganglia of both sides.

Epilepsy, encephalitis, and Guillain-Barré syndrome were the primary diagnoses; therefore, electroencephalography (EEG) and MRI were carried out. The EEG reported normal function of the brain; nevertheless, MRI revealed basal ganglia damage due to hypoxia; however, their first imaging was normal. Finally, delayed hypoxic encephalopathy was diagnosed in the cases due to methadone poisoning. Both patients were treated with methylprednisolone, vitamin C, coenzyme Q, intravenous immune globulin, L-carnitine, bipyridine, and haloperidol. The sign and symptoms of the first patient after the treatment improved significantly; however, the second case had no improvement (Figures 3 and 4).



Figures 1 and 2. *The imaging of the first case in her second (Left-CT) and third(Right-MRI) admission*



Figures 3 and 4. *The imaging of the second case in her first (Left-MRI) and second (Right- MRI) admission*

Discussion & Conclusion

To the best of our knowledge, this is the second and third report of delayed hypoxic encephalopathy after methadone poisoning in children (6). A similar circumstance occurs in a 30-month-old baby. She was accidentally poisoned by methadone at home. She manifested slurred speech, dystonia, normal gait reflexes, and agitation 5 days after the poisoning. At this time, the imaging of her brain was normal. The EEG demonstrated generalized slow activity. Lorazepam and clonazepam improved the neurologic manifestations. A lesion was reported in her MRI in the basal ganglia area 19 days after her poisoning. After 5 months, she developed seizures and atrophy of basal ganglia in her MRI (6).

Both our cases had weakness in extremities, abnormal movement of limbs, and slurred speech. Similarly, the above-mentioned case had slurred speech but had gait and dystonia that did not manifest in none of our cases. In these three cases, brain imaging was normal at the time of their first admission. The delayed hypoxic damage in our first case manifested 31 days, in our second case 8 days, and in the case explained above 5 days after methadone poisoning.

The receptors of opioids and methadone are mostly localized in the frontal cortex, hippocampus, cerebellum, and basal ganglia (7). There are several possible mechanisms for these manifestations; firstly, methadone can affect the integrity of white matter (WM) (8); secondly, it can be an appropriate response of the immune system(9); thirdly, some studies suggest that as antioxidant therapy improved the status of the patient, mitochondrial dysfunction might play a role in the damage of the brain (10). As the center of the breathing is in basal ganglia, the methadone affects the WM of this area and can cause hypoxia and hypoventilation, thereby resulting in the hypoxia of the brain and encephalopathy. Additionally, other manifestations can be explained by the aforementioned mechanisms. The older case in our report showed the manifestations of encephalopathy sooner than the younger child. As these children ate the methadone accidentally, the amount of ingested drug cannot be measured to compare these two cases.

The point of this case report is to consider the possibility of encephalopathy after poisoning with methadone, specifically in children, at least 1 and a half months after poisoning and inform the parents that if the child shows the abnormal neurologic symptoms bring it as soon as possible to a hospital for the prevention of the irreversible damages of the brain.

List of abbreviations

ER: emergency room

CT: computer tomography

MRI: Magnetic resonance imaging

ICU: intensive care units

GBS: Guillen Barre syndrome

EEG: electroencephalogram

WM: white matter

Declarations

Ethics approval: This study was reported according to ethics committee of Shiraz University of medical scinces's guidelines.

Consent for publication: The results of this study are reported anounymosly and informed consent was obtained from the patients and families.

Availability of data and materials: The datasets used and/or analysed during the current study are available on reasonable request

Author's contribution

FK and SA wrote the first draft and revised the

final version; SI developed the idea and revised the final version

Acknowledgement

Not applicable

Conflict of interest

There is no confilict of interest for declariation

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