

Can You Repeat What You Just Said? A Case of Unusual Hearing Loss

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Received April 2, 2021; Accepted for publication May 19, 2021; Published online Oct. 14, 2021
<https://doi.org/10.17161/kjm.voll4.i5.331>

INTRODUCTION

Synthetic opioids are a class of psychoactive drugs that are designed to relieve pain. Synthetic opioids are constructed so that they have a base structure that is akin to naturally derived opiates and have similar effects.¹ These include drugs such as fentanyl, methadone, and tramadol among others. Synthetic opioids have significant advantages over naturally derived opiates including decreased cost, higher potency, and faster production speed, however they are not without drawbacks.

As of 2017, an estimated two out of three opioid-involved overdose deaths involved synthetic opioids.² While overdose deaths already were increasing in the months preceding the 2019 novel coronavirus disease (COVID-19) pandemic, the latest numbers suggested an acceleration of synthetic opioid overdose deaths during the pandemic.³ The classic signs of opioid intoxication include altered mental status, decreased respiratory rate, decreased tidal volume, decreased bowel sounds, and miosis.

This report presents a rare case of a young patient who developed toxic leukoencephalopathy and transient hearing loss after a presumed synthetic opioid overdose. The purpose of this case report was to draw attention to these less common complications and provide a review of the literature.

CASE REPORT

A 19-year-old male with history of depression, substance use disorder, and a previous suicide attempt presented to the burn care unit by emergency medical services after being found at home with severely altered mentation, a scald wound on the chest, and possible aspiration pneumonia following ingestion of an unknown substance. On arrival, he was unresponsive and would not follow commands. He had crackles in the bases of the left lung with oxygen saturation at 74%, he was covered in urine and feces, and had an estimated total body surface area burn of 6% to the chest with blistering. Due to significant distress, the decision was made to intubate. Urine drug screen on admission was positive for cannabis, but negative for any other illicit substances. Other labs, including complete blood count, comprehensive metabolic panel, and urinalysis, were unremarkable except slightly elevated liver function tests and lactic acid. Initial computed tomography (CT) of the chest showed a focal consolidation in the left lower lobe consistent with aspiration pneumonia and initial head CT without contrast was negative for acute processes. An electrocardiogram showed sinus tachycardia. He remained intubated for the next 24 hours while his burns and aspiration pneumonia were addressed by surgical and pulmonary teams.

The patient's mother was contacted for past medical history and potential substances ingested. She was unaware of the patient's recent whereabouts or what he may have ingested prior to current admission. His mother reported an overdose four months prior on benzodiazepines,

cocaine, marijuana, and a synthetic blend of fentanyl and oxycodone/acetaminophen. She stated that the patient was involved in "research chemicals" that he ordered over the internet. The patient's psychiatric history included one inpatient hospitalization for suicidal ideation as an adolescent, two previous suicide attempts, prior incarceration for battery of an officer, and a history of depression. At presentation, he was not being treated for his depression and had no outpatient psychiatrist.

Following extubation on the second day of admission, his mental status remained severely altered. He would open his eyes in response to sternal rub, but would not follow commands and remained nonverbal. He continued to be incontinent of urine and feces. On day three, the patient started communicating verbally; however, speech was nonsensical, and he appeared to be responding to internal stimuli. He was not oriented to time, place, or situation.

With lack of improvement of his mentation by day six, the psychiatry service was consulted. Their working diagnosis was unspecified schizophrenia spectrum and other specified disorder, synthetic opioid withdrawal psychosis, or anoxic brain injury due to toxic ingestion. Magnetic resonance imaging (MRI) of the brain was ordered to rule out underlying causes. In addition, risperidone 1 mg twice daily was started for agitation and aggression toward staff.

The MRI of the brain showed symmetric bilateral diffusion restriction with fluid-attenuated inversion recovery (FLAIR) abnormality in the centrum semiovale, occipital lobes, and splenium of corpus callosum consistent with anoxic brain injury. A lumbar puncture was negative. A diagnosis of toxic leukoencephalopathy likely caused by an overdose on a synthetic opioid such as fentanyl was established.

The patient's mentation improved over the following days. He was oriented to self and was able to feed himself for the first time. Physical therapy evaluation noted significant motor impairments with persistent posterior lean on standing, inability to take more than two steps with the help of a walker, and severe balance impairment with a left lower extremity limp.

On day 13, the patient was evaluated again by the psychiatry team. He was oriented to time, location, and person for the first time. He was able to maintain a full conversation and admitted to overdosing on a "pressed pill" at a friend's house before waking up in the hospital. He stated that these pills were manufactured in Mexico and often contain synthetic opioids. He reported that this was the first time when he could remember anything prior to his overdose. He was unaware how long he had been in the hospital.

Further evaluation revealed overall improvement in his cognition. However, the patient was noted to have significant hearing impairment, as evidenced by asking the care team to repeat multiple questions at a significantly louder volume. He was able to hear low pitch volumes better than higher pitch. This was noted to be a new deficit that he did not have prior to current hospitalization. The initial differential for his sudden bilateral hearing loss included encephalitis, tumor, noise-induced loss, autoimmune disorder, and/or ototoxic medications;

however, all were eventually ruled out. Extensive workup for encephalitis was unremarkable and a brain MRI did not show evidence of a tumor or autoimmune disease such as multiple sclerosis. There was no collateral information indicating he was exposed to a loud/long lasting noise and was not prescribed any medications that are typically ototoxic.

Two weeks following admission, risperidone was stopped. He no longer had visual or auditory hallucinations, was alert and oriented, and reported to be at his cognitive baseline. The remainder of patient's hospital course was complicated by fevers with left forearm cellulitis and thrombophlebitis which prolonged his hospital stay. The patient's hearing slowly improved. After stabilization and resolution of his infection, he was discharged home 24 days after admission.

DISCUSSION

Ototoxicity and toxic leukoencephalopathy are known, albeit rare, distinct complications of synthetic opiate overdose.^{4,13} To our knowledge, this is the first reported case in which these complications have co-occurred.

Despite the prevalence of opioid abuse, a relatively small number of cases of leukoencephalopathy as the result of inhalation, intravenous injection, or ingestion of opioids have been reported.⁴ The most studied cause of toxic leukoencephalopathy has been the inhalation of heroin, colloquially known as "chasing the dragon", and has been recognized since the 1980s. About 160 cases have been documented as of 2018. Cases also have been reported as a result of abusing other opioids such as methadone, oxycodone, and fentanyl, though these occurrences appear to be rarer.

Clinical features of toxic leukoencephalopathy secondary to opioid overdose may include the following: cerebellar dysfunction, confusion, motor restlessness, mutism, and/or incontinence, though no particular symptom is considered pathognomonic.⁵⁻⁷ The pathogenesis of neurologic injury related to opioid overdose is unknown. One theory suggested mitochondrial dysfunction may play a role, as mitochondrial changes have been seen histologically on brain biopsy specimens.⁵ The diagnosis should be suspected in patients with a history of substance abuse, especially a history of opioid abuse. A urine drug screen can be helpful, but synthetic opioids often do not show up on a standard screen; therefore, history that can be confirmed by reliable collateral sources can provide diagnostic value. Brain MRI commonly shows diffuse, symmetrical hyperintensities on T2 and FLAIR sequences, affecting primarily white matter, and the frontal lobes are relatively spared.⁷ There was some evidence that giving antioxidants (e.g., CoQ, vitamin C, vitamin E) may result in varying levels of improvement, however, data are limited and had mixed results.⁸⁻¹¹

Sensorineural hearing loss is another unusual complication of an opioid overdose.¹² Symptoms can be as mild as transient tinnitus and can be as severe as permanent deafness. It has been associated with several mu receptor agonists including heroin, oxycodone, methadone, and tramadol, among others. The exact mechanism of opioid induced

hearing loss is unknown, but theories included ischemic cochlear injury secondary to artery vasospasm, abnormalities in transporting proteins and receptors, and/or direct effect of opioids on opioid receptors.¹³

The cochlea is a highly metabolic structure and distinctly susceptible to ischemia. Opioids stimulate production of endothelin-1, an endogenous vasoconstrictor, theoretically leading to vasospasm and cochlear ischemia.¹³ The blood-labyrinth barrier maintains homeostasis of inner ear fluid. Variation in the permeability of this barrier between opioid users, according to differences in the molecular weight of opioid drugs, may contribute to opioid induced hearing loss. Finally, opioid receptors (mu, kappa, and delta) are present in the inner ear, although their physiologic role here is not determined. Endogenous opioid peptides likely play a role in auditory neuromodulation and it is possible that activation of these receptors by an exogenous opioid may impair this process and lead to hearing loss.

The clear majority of opioid associated hearing loss cases are bilateral.¹² In a retrospective review of 41 cases reporting hearing loss after opioid overdose in New Jersey Poison Center records over the last two decades, 12 reported complete deafness, 15 reported hypoacusis, 10 reported tinnitus, and 4 cases reported mixed auditory dysfunction. Of these cases, 7 reported complete resolution, 8 reported partial resolution, 4 reported no resolution, with the remainder not including resolution data. Another theoretical cause of hearing loss after opioid overdose was hypoxia related to respiratory suppression, however, 61% of the 41 cases reported no presence of a hypoxic event after their overdose, making this etiology less likely, or perhaps a secondary contributor to hearing loss.

This case revealed two rare complications of synthetic opioid overdose that should be kept on the differential diagnosis for patients who present with altered mental status, especially younger patients with history of substance abuse. This case was relevant given the increasing rate of synthetic opioid overdose in the United States and increasing need for awareness of potential overdose sequelae.¹⁴ We propose that both toxic leukoencephalopathy and hearing loss likely were under-reported phenomena associated with synthetic opioid overdose and suggest additional case reports and epidemiological studies be done to elicit their rate of incidence further.

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Keywords: opioids, synthetic drugs, hearing loss, leukoencephalopathy, drug overdose