A Case Report of Myelopathy Following Heroin Overdose in a Child

Ana Melikishvili, MD1, Bijal Patel, MD2, Daphne M. Hasbani, MD, PhD2, and Karen S. Carvalho, MD2

Abstract
Neurologic complications secondary to heroin abuse in the adult population have been widely described in the literature. With the recent opioid epidemic and increasing rates of heroin abuse in adolescents, pediatricians are now encountering the diagnostic and management challenge of similar complications in children. We report a case of a 16-year-old girl who presented with complete paraplegia after a heroin overdose. Spinal magnetic resonance imaging showed diffuse thoracic spinal cord abnormalities. She rapidly recovered after high dose intravenous corticosteroids and, upon hospital discharge 2 weeks later, required minimal assistance with ambulation. This case represents the youngest patient reported with the rare complication of myelopathy associated with heroin use.

Keywords
myelopathy, heroin, overdose

Received January 14, 2021. Received revised June 16, 2021. Accepted for publication June 18, 2021.

Introduction
Heroin is one of the most widespread recreational drugs available. Amid the current national opioid crisis we are seeing a rapid increase in opioid abuse in teenagers and young adults of all races and socioeconomic status. Heroin, or diacetylmorphine, is a semi-synthetic opioid derived from the poppy plant that can be administered through injection routes (intravenous [IV], intramuscular, or subcutaneous) or through non-injection routes (snorting or swallowing). Users quickly develop dependence and tolerance to the drug. Exposure to heroin is associated with several neurologic complications. Central nervous system (CNS) demyelination has been described with chronic heroin use. Hypoxia is often seen in acute overdose. Ischemic stroke can occur due to either vascular hypersensitivity/arteritis or infective endocarditis and embolism caused by add-on ingredients. CNS infections of varied pathogens have been described with IV drug use. Spongiform leukoencephalopathy appears to be specifically related to inhalation of pre-heated heroin. Acute myelitis has also been described as a rare complication of intravenous and intranasal heroin use in young adults, often following a period of drug abstinence. The pathophysiology and prognosis of heroin-induced myelopathy is unclear.

We discuss the case of a 16-year-old girl who presented with acute complete paraplegia after heroin overdose.

Case Report
A 16-year-old girl with a history of polysubstance abuse, anxiety, depression, and obsessive-compulsive disorder was found unconscious after a self-reported heroin overdose. She recalled using 2 bags of heroin intravenously prior to loss of consciousness. The exact duration of downtime prior to medical intervention was unknown but was suspected to be at least 4 hours prior to arrival of emergency medical services (EMS). She regained consciousness following naloxone administration by the emergency room physician, whereupon she was aware of...
weakness and loss of sensation in her bilateral lower extremities. Urine drug screen was positive for opiates and cocaine. Four hours after arrival to the emergency room, the patient started displaying withdrawal symptoms including tremor, agitation, and body aches. Her neurological examination showed normal motor strength of her facial and upper extremities muscles with complete paraplegia of her lower extremities. She had symmetric and normal deep tendon reflexes of her biceps, triceps, and brachioradialis with absent patellar and achilles deep tendon reflexes and mute plantar responses. Sensation to touch and cold temperature was diminished below the level of T7-T8. Vibration and joint proprioception were preserved. She had a normal mental status, cranial nerves, and cerebellar exam. Her examination was consistent with a grade B spinal cord injury per the American Spinal Injury Association (ASIA) impairment scale.\textsuperscript{13} Spine magnetic resonance imaging (MRI) showed a diffuse longitudinally extensive signal intensity alteration involving the spinal cord from T3 to T11 (Figure 1).

Cerebrospinal fluid (CSF) analysis showed normal cell counts, protein, and glucose with negative bacterial culture. CSF myelin basic protein (MBP) was elevated at 29.8 ng/mL (normal <1.2 ng/mL). With these findings, the diagnosis of acute transverse myelitis was made. She was treated with 1 gram/day IV methylprednisolone for 3 days. She showed steady improvement in her neurologic symptoms over the next several days. Upon discharge to a rehabilitation center 2 weeks from admission, she had improvement in her lower extremity weakness with spontaneous antigravity movement and resolution of sensory deficits aside from a band at the level of her umbilicus. She was able to ambulate with a walker but continued to have a neurogenic bladder requiring intermittent catheterization. The neurological examination was consistent with a grade D spinal cord injury per the ASIA impairment scale and a modified Rankin Scale (mRS) score of 4.

Discussion

Myelopathy related to heroin overdose has been reported mostly in young adults. Our patient is the youngest patient with this complication reported to our knowledge. The pathophysiology of heroin-induced myelopathy is poorly understood, and both inflammatory and ischemic mechanisms have been postulated. Because myelopathy following heroin use commonly occurs after a period of abstinence, there has also been widespread thought that a hypersensitivity reaction to heroin may be involved, indicating an immunological process.\textsuperscript{3–5,10} Mahoney et al reported a young adult with heroin-induced myelopathy who had CSF pleocytosis with evolution from a neutrophilic to a lymphocytic predominance, suggesting an acute inflammatory process.\textsuperscript{14} Furthermore, spinal angiography suggested vasculopathy given the findings of a normal artery of Adamkiewicz but a pronounced capillary blush at cervical and conus medullaris levels with prominent early venous return and irregular caliber of the anterior and posterior spinal arteries. The presence of an ischemic component likely contributed to this patient’s poor response to steroids and immunomodulators.\textsuperscript{14} Some authors have suggested that, in cases where patients were found unconsciousness, systemic hypotension and cord ischemia may play a major role in the pathogenesis of spinal cord injury rather than heroin-induced neuroinflammation. This hypothesis seems to be particularly supported by the presence of myelitis in the thoracic “watershed” area of the cord.\textsuperscript{3,5} It is also known that heroin causes histamine release. Although less common, this may lead to histamine mediated tachycardia and a dilatory effect on small blood vessels leading to flushing, decreased vascular resistance and hypotension, ultimately leading to hypoperfusion of the spinal cord.\textsuperscript{15} Another possibility is a direct toxic effect of heroin on neural tissue, especially in cut heroin. Sveinsson et al claimed that very high levels of glial fibrillary acidic protein (GFAP) in the CSF of a patient with heroin-induced myelopathy suggested the possibility of heroin causing direct astrocyte injury.\textsuperscript{10} It is likely that different mechanisms including immune-mediated hypersensitivity, direct and

![Figure 1](image-url)
indirect toxicity, vasculopathy or vasculitis, and hypotension play varying roles in individual patients.

The absence of diffusion restriction on MRI would argue strongly against an ischemic mechanism. Unfortunately, diffusion weighted imaging was not performed with initial spine MRI in our patient and consent was denied for a repeat MRI. Spinal cord infarctions are often devastating with poor functional outcome and meaningful recovery commonly takes months to years. We reviewed the Zalewski diagnostic criteria for a spinal cord infarction (SCI) which emphasizes 3 major components: rapid development of severe deficits within 12 hours, MRI of the spine with exclusion of compression with supportive SCI features, and noninflammatory CSF findings. Zalewski et al specify “the most critical component is the rapid accumulation of severe deficits within 12 hours because more gradual worsening favors alternative etiologies.” The time course of development of neurologic deficits could not be confirmed by our patient, limiting the applicability of the Zalewski criteria to our patient. Moreover, elevated MBP, the presence of more diffuse spinal cord abnormal signal, and rapid recovery after a short steroid course favors inflammation over an ischemic process.

Urine drug screen for our patient was positive for cocaine as well. There are several reports of cocaine-related acute spinal cord infarction. Although it is uncommon, it is described to primarily involving the anterior spinal cord artery and the prognosis is more guarded with additional significant neurological sequelae.

Treatment of heroin-induced myelopathy is largely supportive. Intravenous corticosteroids and immunomodulators such as plasma exchange have been used with no supporting data. While outcomes from post-infectious transverse myelitis have been well-reported, the paucity of heroin-induced myelopathy cases, particularly in the pediatric population, makes correlations between age of the patient and recovery difficult.

There were several limitations in the findings we report. Given the patient’s history of polysubstance abuse, we cannot exclude the possibility of separate toxic metabolic processes as contributors to her clinical presentation. Furthermore, it is well known that heroin is often cut with other substances which may mimic or enhance the effects. A comprehensive drug screen was not sent to rule out the presence of other substances. The differential for her presentation also includes other demyelinating conditions which may mimic transverse myelitis, such as Neuromyelitis Optica spectrum disorder and Myelin oligodendrocyte glycoprotein related disorders. However, the relevant studies (AQP4 Ab and MOG Ab) were not performed in our patient. Additionally, follow up imaging and neurological examination would have aided in management and understanding of her clinical presentation, but she was lost to follow up.

With widespread use of opioids among all ages and socioeconomic classes, physicians need to be aware of the neurologic complications of heroin use. While rare, myelopathy following heroin use can be seen in children and pediatricians should be familiar with the signs and symptoms of this condition. Larger case series are needed for better delineation of the pathophysiology, treatment, and prognosis of heroin-induced myelopathy.

Author Contributions
All authors contributed to conception, design, acquisition, analysis, and interpretation; drafted the manuscript; critically revised the manuscript; gave final approval; and agrees to be accountable for all aspects of work ensuring integrity and accuracy.

Declaration of Conflicting Interests
The author(s) declared no potential conflicts of interest with respect to the research, authorship, and/or publication of this article.

Funding
The author(s) received no financial support for the research, authorship, and/or publication of this article.

ORCID iD
Bijal Patel, MD  https://orcid.org/0000-0002-8893-3483

Ethics Approval
Our institution does not require ethical approval for reporting individual cases or case series.

Informed Consent
Informed consent for patient information to be published in this article was not obtained because patient was lost to follow up.

References
1. White E, Comiskey C. Heroin epidemics, treatment and ODE modelling. Math Biosci. 2007;208(1):312-324.
2. Büttner A, Mall G, Penning R, Weis S. The neuropathology of heroin abuse. Forensic Sci Int. 2000;113(1-3):435-442.
3. Ell JJ, Uttley D, Silver JR. Acute myelopathy in association with heroin addiction. J Neurol Neurosurg Psychiatry. 1981;44(5):448-450.
4. Pearson J, Richter RW, Baden MM, Challenory JB, Brunn B. Transverse myelopathy as an illustration of the neurologic and neuropathologic features of heroin addiction. Hum Pathol. 1972;3(1):107-113.
5. Richter RW, Pearson J, Brunn B, Challenory JB, Brust JC, Baden MM. Neurological complications of addiction to heroin. Bull NY Acad Med. 1973;49(1):3-21.
6. Caplan LR, Hier DB, Banks G. Current concepts of cerebrovascular disease—stroke: stroke and drug abuse. Stroke. 1982;13(6):869-872.
7. Kelly MA, Gorelick PB, Mirza D. The role of drugs in the etiology of stroke. Clin Neuropharmacol. 1992;15(4):249-275.
8. Celius EG, Andersson S. Leucoencephalopathy after inhalation of heroin: a case report. J Neurol Neurosurg Psychiatry. 1996;60(6):694-695.
9. Sahni V, Garg D, Garg S, Agarwal SK, Singh NP. Unusual complications of heroin abuse: transverse myelitis, rhabdomyolysis, compartment syndrome, and ARF. Clin Toxicol (Phila). 2008;46(2):153-155.
10. Sveinsson O, Herrman L, Hietala MA. Heroin-induced acute myelopathy with extreme high levels of CSF glial fibrillar acidic protein indicating a toxic effect on astrocytes. *BMJ Case Rep*. 2017;2017:bcr2017219903.

11. McCreary M, Emerman C, Hanna J, Simon J. Acute myelopathy following intranasal insufflation of heroin: a case report. *Neurology*. 2000;55(2):316-317.

12. Dujmovic I, Nikolic I, Martinovic V, Mesaros S, Drulovic J. Heroin-induced acute longitudinally extensive transverse myelopathy. *Neurol Sci*. 2018;39(4):791-792.

13. Kirshblum SC, Burns SP, Biering-Sorensen F, et al. International standards for neurological classification of spinal cord injury (revised 2011). *J Spinal Cord Med*. 2011;34(6):535-546.

14. Mahoney KW, Romba M, Gailloud P, Izbudak I, Saylor D. Acute progressive paraplegia in heroin-associated myelopathy. *J Clin Neurosci*. 2018;51:69-71.

15. Baldo BA. Toxicities of opioid analgesics: respiratory depression, histamine release, hemodynamic changes, hypersensitivity, serotonin toxicity. *Arch Toxicol*. 2021.

16. Robertson CE, Brown RD Jr, Wijdicks EF, Rabinstein AA. Recovery after spinal cord infarcts: long-term outcome in 115 patients. *Neurology*. 2012;78(2):114-121.

17. Zalewski NL, Rabinstein AA, Krecke KN, et al. Characteristics of spontaneous spinal cord infarction and proposed diagnostic criteria. *JAMA Neurol*. 2019;76(1):56-63.

18. Farrell CM, Cucu DF. Cocaine-related acute spinal cord infarction. *R I Med J (2013)*. 2018;101(1):28-29.

19. Williamson J, Bonello M, Simpson M, Jacob A. Spinal cord infarction after cocaine use. *Pract Neurol*. 2017;17(1):51-52.

20. Schreiber AL, Formal CS. Spinal cord infarction secondary to cocaine use. *Am J Phys Med Rehabil*. 2007;86(2):158-160.

21. Sawaya GR, Kaminski MJ. Spinal cord infarction after cocaine use. *South Med J*. 1990;83(5):601-602.