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Case Report OMICS International

Toxic Leukoencephalopathy and Delayed Neuropsychosis after Opioid Overdose

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Abstract

First time neuro-psychiatric disorders in the emergency department present a challenging and broad differential. Physicians often anchor on recent substance abuse as a possible cause of acute mental status change. Overlooked, however, is the occurrence of delayed sequelae as a result of a severe intoxication. This article describes the occurrence of neurologic injury at a delayed interval following an opioid induced episode of prolonged unresponsiveness.

Keywords: Delayed post-hypoxic leukoencephalopathy syndrome; Chasing the dragon; Spongiform leukoencephalopathy; Leukodystrophy; Opioid overdose

Introduction

Leukoencephalopathy refers to the broad spectrum of diseases involving white matter of the brain, characterized in particular by damage to myelin. Toxic leukoencephalopathy, or toxic spongiform leukoencephalopathy, describes the pathologic result of chemical or environmental exposures either by direct neurotoxin effect, or by alterations in cerebral perfusion or oxygenation. Historically, cases of toxic leukoencephalopathy were observed in cancer patients after cranial irradiation or use of anti-neoplastic drugs [1]. Histologic analysis can reveal damage to any cell line within white matter, but commonly demonstrates myelin disruption with lipid filled macrophages resulting in the characteristic "spongiform" appearance [2]. Clinical presentations of these white matter changes can include cognitive deficit, neuro-motor alterations, and neuro-psychiatric manifestations of bizarre behaviour [3].

Similar pathologic changes and clinical syndromes have been observed secondary to substance abuse and prolonged states of hypoxia. Heroin use by way of inhalation, or "chasing the dragon" as it is known, has been linked to fatal neurobehavioral deteriorations [4,5]. While the mechanism is still unclear, it is speculated that toxins from the pyro lysate vapour that arises from heating heroin on tin foil may be directly neurotoxic to myelin. An alternative explanation points to respiratory depression and decreased cerebral perfusion as the cause for cell damage. Delayed post-hypoxic leukoencephalopathy syndrome has been defined as a demyelination occurring after prolonged hypoxia such as carbon monoxide poisoning, sedative overdose, or anoxic brain injuries [6,7].

Case Report

A 43-year-old woman presented to the emergency department with a gradual deterioration in cognitive function and worsening bizarre behaviour. She had experienced a fall from standing three weeks prior to presentation during which she struck the back of her head, however did not require or pursue medical attention. She had also recently experienced the death of her mother. Her husband observed initially that she began to experience memory loss and confusion, but that she quickly progressed to strange behaviours including brushing teeth with a hair brush, showering while fully clothed, and leaving her home undressed. She had a history of depression and anxiety for which she had been on SSRIs and alprazolam, and was known to have a history of heavy alcohol use. Family was concerned that her recreational substance abuse had increased following the passing of her mother.

The patient was admitted to a medicine service for further evaluation of altered mental state. Non-contrast computed tomography (CT) of the head and initial laboratory testing was unremarkable. Urine drug screening and serum alcohol testing were negative. On exam, she was able to carry a conversation and follow basic commands; however she was intermittently disoriented and unable to write her name. She exhibited childlike behaviour, but was easily re-directable. At the same time, she had insight and knew that her behaviour might be perceived as strange to people around her. Electroencephalogram (EEG) showed mild slowing concerning for encephalopathy. Cerebral spinal fluid (CSF) analysis was normal and unrevealing. Magnetic resonance imaging (MRI) of the brain showed diffuse supra-tentorial white matter signal changes consistent with encephalitis or toxic-metabolic abnormalities (Figure 1).

A week into her admission, the patient developed fevers, experienced acute deterioration of her mental status, and was observed to have episodes of generalized shaking and rigidity. She developed autonomic instability with persistent tachycardia and generalized posturing concerning for unsecure respiratory status and possible seizure activity, resulting in intubation. IR angiogram was negative for vascular pathology. With laboratory testing for infectious, metabolic, and toxic causes negative, the patient subsequently underwent brain biopsy. Pathologic analysis demonstrated spongiform leukoencephalopathy. The patient was transitioned to comfort care and expired shortly after.

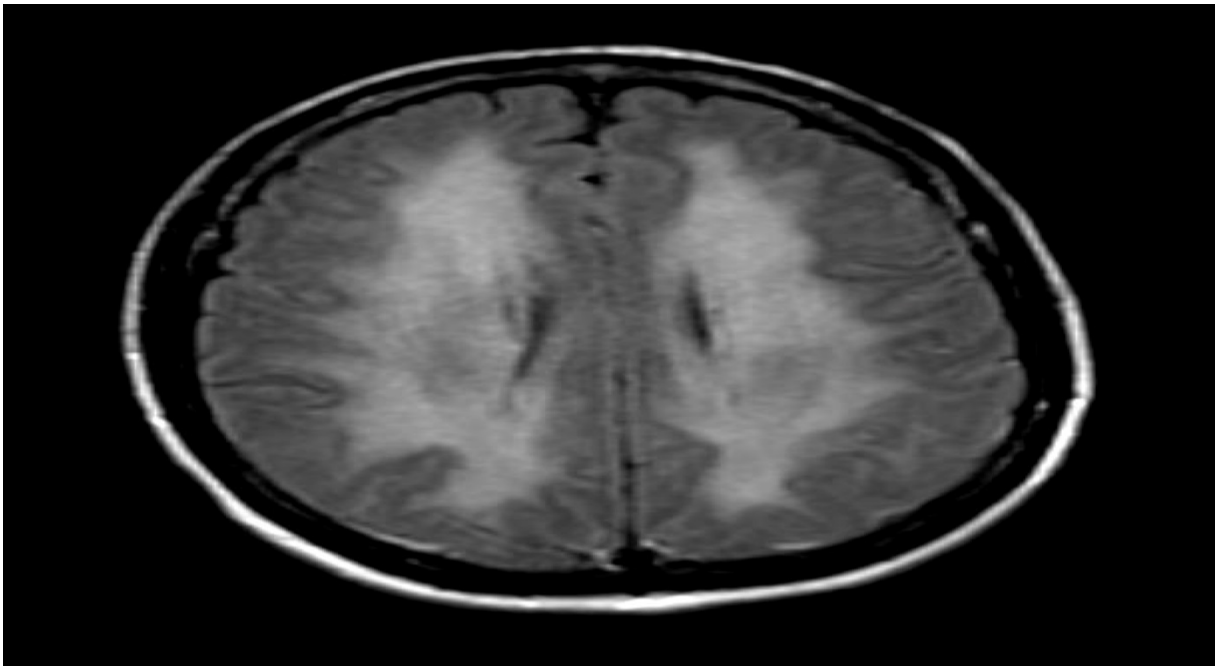

Figure 1: Magnetic resonance imaging (MRI) showing signal loss in large areas of white matter.

Discussion

The patient was diagnosed with toxic spongiform leukoencephalopathy following anatomic pathology analysis consistent with white matter changes seen in substance abuse cases such as "chasing the dragon syndrome." There were no indications that the patient had inhaled narcotics. However, throughout the course of her hospitalization, several family and friend accounts revealed further the degree of the patient's substance abuse. For her depression and anxiety, the patient had long history of various benzodiazepine prescriptions and was accustomed to drinking multiple alcoholic beverages daily. She did so while maintaining a steady job and the semblance of a normal social life. Prior to her fall and onset of symptoms, the patient had experienced the sudden passing of her mother. It was noted that she had collected several bottles of her mother's opioid medications, had become intoxicated, and was observed recreationally using these medications. One night in particular, it was reported that she had a prolonged stupor of 16-20 hours. Days after this occurrence she experienced the fall from standing which did not result in serious injury. In the weeks prior to presentation, she was fully functional until she began to exhibit bizarre behaviours as noted above.

A period of lucidity has been recognized previously in cases of delayed post-hypoxic leukoencephalopathy [8,9]. While the pathophysiology remains unclear, there is evidence to suggest that myelin sheath will degrade over a longer period of time from the hypoxic exposure as compared to other glial cells [10]. Furthermore, it has been suggested that certain patients may be pre-disposed to this type of white matter injury as a result of decreased arylsulfatase activity, which leads to leukodystrophy [11]. A "two hit" theory has been proposed to explain why leukoencephalopathy does not result at higher incidence rates given the degree of sedative abuse cases seen [12].

Our patient had several risk factors for the development of leukoencephalopathic changes. She acquired an unknown supply of opioid medications from her mother and had access to benzodiazepines as well. While she did not fatally overdose during the night she was observed to be intoxicated, she likely experienced a prolonged hypoxic and hypo-perfusion state which led to delayed demyelination resulting in spongiform leukoencephalopathy. Furthermore, the fall may have been a "second hit" of sorts that, through other concussive pathways, may have exacerbated her underlying hypoxic injury. Alternatively, the acute intoxication at her mother's funeral may have worsened existing neurologic insult from her chronic substance abuse over previous years.

In November of 2016, the Surgeon General released a report addressing the on-going epidemic of substance abuse in America, stating that more than 21 million Americans are affected by addiction [13]. Emergency department visits for substance abuse continue to increase, and death rates from traditional drugs of abuse remain, or as with heroin continue to rise [14]. As the issue of substance abuse continues, attention should be given to the long term health consequences of non-fatal but severe overdose, including neuropsychiatric complications.

Conclusion

It is common to focus on acute intoxications in the emergency department as a possible explanation for psychiatric presentations. This is especially true when dealing with first time psychosis in patients beyond the typical age range for developing psychiatric conditions. Neuropsychiatric sequelae from hypoxic periods should be considered for patients with new behavioural changes after non-fatal drug abuse or overdose.

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