

Toxic Leukoencephalopathy due to Inhalational Heroin Abuse

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Abstract

Heroin-induced spongiform leukoencephalopathy (HSLE) is a rare condition that is strongly associated with heroin vapor inhalation which has become a popular method among heroin addicts because it poses a less immediate danger to the user and makes the drug much easier to use. We present a case of a 22-year-old male who presented with dysarthria and cerebellar symptoms starting, after 3 months of heroin inhalation. Diagnosis was confirmed to be HSLE after extensive diagnostic testing. HSLE is a rare complication of which the pathogenesis is poorly understood. Clinical history and characteristic findings on magnetic resonance imaging (diffuse, symmetric T2-hyperintensity, and diffusion restriction in frontal, parietal, occipital lobes, basal ganglia, and superior cerebellum) are diagnostic; however, care should be taken to exclude other etiologies. Treatment is primarily supportive; however, there is anecdotal evidence that coenzyme Q10 may be of benefit. The growing number of victims of the opioid crisis requires that physicians be aware of and counsel patients on the devastating neurological complications that can occur with abuse of these drugs.

Keywords: Drug abuse, encephalopathy, heroin

INTRODUCTION

From 2010 to 2014, the number of opioid-related deaths tripled, sparking a National call to action in the United States to curbing this epidemic.^[1] Heroin-induced spongiform leukoencephalopathy (HSLE) is a rare condition that is strongly-associated with heroin vapor inhalation which has become a popular method among heroin addicts because it poses a less immediate danger to the user and makes the drug much easier to use. This mode of heroin injection – “chasing the dragon” - involves heating the powder on a thin foil and inhaling the vapor.^[2-4] It eliminates the danger of contracting HIV, hepatitis, and other diseases that result from sharing needles. The majority of reported HSLE comes from heroin vapor inhalation. However, there have been cases where toxic leukoencephalopathy was associated with heroin injection and intranasal administration.^[3-5] A recent survey conducted in 2015 shows that this mode of abuse is on rise with an increase to over 30% from 11.5%.^[6]

CASE REPORT

A 22-year-old male with no prior medical history presented to our institution’s emergency department with 5 days of progressively worsening difficulty with walking and slurred speech. The patient also reported flu-like symptoms such as a headache, nausea, myalgias, and generalized weakness for the past week. He denied numbness and tingling of the extremities. He reported worsening twitching of his extremities over the past 3 months. He reported daily heroin abuse through inhalation for three years but reported no intravenous use. Computed tomography of the head revealed multiple moderate size areas of abnormal hypodensity in the bifrontal, parietal, temporal, and occipital lobes, as well as cerebellum and basal ganglia [Figure 1]. Complete blood count and chemistry were within the normal limits. Urine drug screen was positive for opiates and methamphetamines. Electrocardiogram showed

normal sinus rhythm. He exhibited no signs or symptoms of opioid withdrawal. The patient was subsequently admitted to the floor for observation and neurology consultation was requested. Neurological examination revealed subtle abnormalities. Cranial nerves II-XII were normal. In particular, there was no nystagmus. Motor examination showed essentially 5/5 strength; however, the tone and resistance were diminished compared to that expected of a healthy 22-year-old male. Deep tendon reflexes were all normal. The plantar responses were flexor. Sensation to light touch was intact. Cerebellar examination showed ataxia and dysidiadochokinesia bilaterally.

A magnetic resonance imaging (MRI) of the brain with and without contrast was performed which showed abnormal signal involving the bilateral periventricular white matter, basal ganglia, brain stem, and superior cerebellum - suggestive of a metabolic process [Figure 2]. HIV, HBV, HCV, and venereal disease research laboratory (VDRL) serologies returned the negative. A lumbar puncture demonstrated a normal opening pressure. Cerebrospinal fluid was sent for cell count, glucose,

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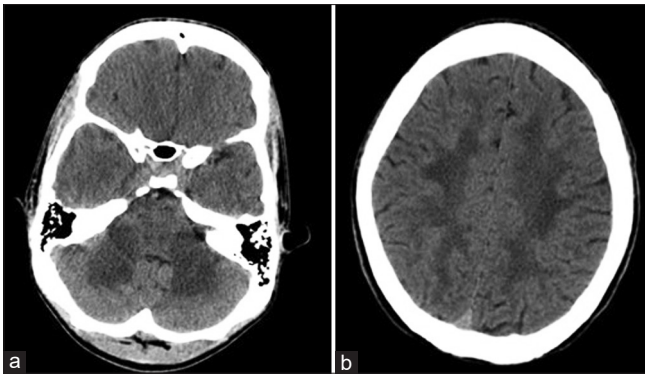


Figure 1: (a) Axial Computed tomography of our patient showing symmetric hypodensities in the superior cerebellum bilaterally (b) Symmetric hypodensities seen in the deep white matter tracts in bilateral frontoparietal lobes

protein, coccidioidomycosis, Cryptococcus, VDRL, JC virus, oligoclonal bands, myelin basic protein, immunoglobulin G index, and rapid plasma reagin – all of which were normal.

Given the imaging findings, in conjunction with normal CSF and serological studies and negative family history, HSLE was suspected. Vitamin E, Vitamin C, and coenzyme Q10 were administered to the patient. Due to the patient's condition and need for long-term rehab, the patient was subsequently transferred to an acute rehabilitation facility. At the time of discharge, the patient had not improved symptomatically but had a loss of taste and appetite.

DISCUSSION

Pathogenesis

The exact pathogenesis of HSLE is not perfectly understood. A thorough investigation of 47 patients conducted by Wolters *et al.* failed to find a toxicological cause of HSLE in an autopsy study of 10 patients.^[7] It has been postulated that since the majority of the cases are associated with heroin vapor inhalation, toxins from heroin pyrolysate (the product produced from heating heroin) may be responsible for the condition.^[2,7] There is some evidence that it may induce apoptosis in cerebellar granule cells through the activation of the c-Jun N-terminal kinase/c-Jun pathway. This results in Bim upregulation, which is a likely mediator of heroin toxicity.^[8]

HSLE is characterized by the spongiform degeneration of the white matter with vacuoles surrounded by thin myelinated fibers, reduced number of oligodendrocytes, and reduction of the axons.^[2] It is suspected that a dysfunction of the oligodendrocyte mitochondria and oligodendrocyte apoptosis is associated with HSLE.^[9] As a consequence, HSLE is highly dependent on myelin turnover, and as a result, the slowest myelinating fibers such as the subcortical U-fibers are usually spared.^[10] Opiate receptors have the highest density within the cerebellum. Therefore, more severe demyelination is found in the cerebellum which leads to symptoms such as motor restlessness and cerebellar ataxia.^[11] It is interesting to note that there is usually symmetrical involvement, which indicates

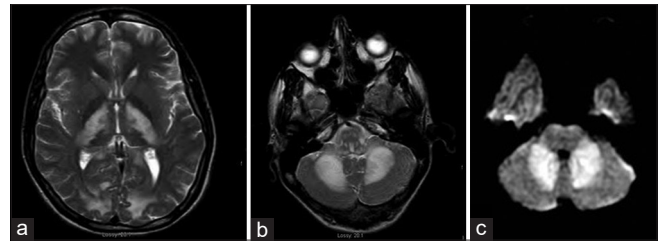


Figure 2: (a) Magnetic resonance imaging T2-sequence of our patient demonstrating symmetric hyperintensity in bilateral basal ganglia, thalami, and occipital lobes. There is sparing of the anterior limb of the internal capsule. (b) Magnetic resonance imaging T2-sequence demonstrating symmetric hyperintensity in the superior cerebellum bilaterally. (c) Magnetic resonance imaging diffusion-weighted imaging sequence demonstrating correlating restricted diffusion with hyperintensity seen on T2

that a toxic or metabolic etiology is involved in HSLE.^[12] Valk and van der Knaap describes “topistic topographical areas” as a region of functional chain of neurons and tracts that show a synchronous development, including myelination.^[13] Demyelination due to degeneration or toxic damage may also be synchronous as seen in HSLE.^[12] A recent study conducted by Yin *et al.* showed that HSLE patients also present with changes in the cerebral blood vessels, which might be another major cause of HSLE. Damage to the cerebral microvasculature may cause reduction in the blood flow in watershed regions and increase the hydrolysis of myelin basic protein - leading to the damage to the myelin sheath in the white matter.^[14]

Presentation

There appears to be a higher incidence of HSLE among males and those of Asian ethnicity. In a review of 27 cases in British Columbia, Buxton *et al.* found that 74% of patients were male and 54% were Asian.^[15] The clinical presentation in HSLE patients varies greatly depending on their clinical stage – latent, intermediate, or vegetative dysregulation.^[9] There is usually a latent period of hours, days, or months before symptoms arise.^[16] HSLE patients generally present with symptoms that belong in one of the three clinical stages. The initial stage includes motor restlessness, apathy, bradyphrenia, cerebellar speech disturbance, and cerebellar ataxia. The intermediate stage marks the rapid worsening of the cerebellar symptoms, hyperactive tendon reflexes, pathologic reflexes, tetraparesis, tremor, myoclonic jerks, or choreoathetoid movements. Vegetative dysregulation with profuse perspiration and central pyrexia indicate the terminal stage. Before death, stretching spasms, hypotonic paresis, and akinetic mutism may occur.^[12]

Diagnosis

Aside from urine drug screen to confirm the presence of drug metabolites, there are no laboratory tests to confirm HSLE. CSF sampling is often nondiagnostic; however, a slight CSF pleocytosis may also occur with the absence of inflammatory CSF findings.^[12] CSF is also negative for oligoclonal bands and JC virus as was the case in our patient. Serology is usually negative for HBV, HCV, and HIV.^[5] HSLE should

be considered a diagnosis of exclusion, and therefore, a broad differential must be considered before the diagnosis. Herpes encephalitis, anoxic brain injury, posterior reversible encephalopathy syndrome, Creutzfeldt–Jakob Disease, progressive multifocal leukoencephalopathy, and autoimmune disease are among the differentials that should be considered. One should only arrive at the diagnosis of HSLE only after all other etiologies have been ruled out.

Imaging

MRI is the gold standard imaging modality to diagnose diseases of the white matter. The characteristic MRI findings in HSLE are diffuse, symmetric T2-hyperintensity and diffusion restriction in bilateral frontal, occipital, basal ganglia, cerebellum, and brainstem. In the case of neurotoxic heroin inhalation, the cerebellum and the posterior limb of the internal capsule are usually involved, but the anterior limb is often spared. These findings, in conjunction with positive inhalational heroin abuse and the absence of any other positive laboratory findings, are considered pathognomonic.^[9,17,18] Additional studies found that MR spectroscopy demonstrates increased lactate, decreased N-acetyl aspartate, and normal choline peak.^[17]

Treatment

There are anecdotal accounts of the treatment options of HSLE.^[9,15,19] Treatment with antioxidants including coenzyme Q was found to be of some benefit.

CONCLUSION

HSLE is a known serious adverse effect of inhalational heroin use and can have devastating neurological consequences; however, the pathogenesis has not been clearly identified. Clinical and imaging findings are the hallmark of the diagnosis. Treatment is primarily supportive; however, coenzyme Q10 supplementation has shown limited benefit. Clinicians should be aware of this complication of heroin use as it is on the rise and they should be prepared to counsel patients accordingly given the ongoing opioid epidemic in the United States.

Declaration of patient consent

The authors certify that they have obtained all appropriate patient consent forms. In the form the patient(s) has/have given his/her/their consent for his/her/their images and other clinical information to be reported in the journal. The patients understand that their names and initials will not be published and due efforts will be made to conceal their identity, but anonymity cannot be guaranteed.

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Conflicts of interest

There are no conflicts of interest.

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