Reversible Delayed Leukoencephalopathy after Heroin Intoxication with Hypoxia: A Case Report

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Abstract- Delayed neurological deterioration after hypoxia is uncommon. Here we report a case of reversible delayed leukoencephalopathy following intravenous heroin intoxication with hypoxia. A 42-year-old man presented disturbed consciousness and unstable hemodynamic status after intravenous heroin injection. He made a good initial recovery after infection control and hemodynamic support. But his neurological condition deteriorated later on and gradually progressed into akinetic mutism and generalized hypertonia within 3 weeks. Prominent leukoencephalopathy was disclosed by magnetic resonance imaging (MRI) of the brain. His general condition improved again in a few months and follow-up MRI revealed regression of the white matter lesion. Early diagnosis of delayed leukoencephalopathy with appropriate supportive treatment may be worthwhile as illustrated by the reported case.

Key Words: Delayed leukoencephalopathy, Heroin, Hypoxia

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INTRODUCTION

Heroin, a diacetyl derivate of morphine, can be taken via intravenous or subcutaneous routes. It can also be smoked, sniffed, or inhaled. Common medical complications of heroin addiction include encephalopathy, transverse myelitis, cerebral infarctions, meningitis, cerebral abscess, mycotic aneurysm, and plexopathy. Delayed leukoencephalopathy is an uncommon complication of heroin addiction. We report a case of reversible delayed hypoxic leukoencephalopathy after intravenous heroin abuse.

CASE REPORT

A 42-year-old jobless man had a history of intravenous heroin addiction for several years. He received methadone replacement therapy since 2007 but still had heroin injection during the course of treatment. He took the last dose of methadone (10 ml) in the morning of March 27th, 2008 and the general course was unremarkable on that day. But he was found unconscious by his father in the next morning (for an uncertain period), and remaining vomitus was noticed around his mouth. He was sent to our emergency department immediately. The

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Glasgow coma score was E1M2V1 on arrival. The initial arterial blood gas showed low PO2 (51.2 mmHg), and his systolic blood pressure (SBP) was around 90 mmHg. The Chest X-ray revealed a pneumonic patch on the right side. Computed tomographic (CT) scan of the brain showed no significantly abnormal findings. He was intubated and on a ventilator and was admitted to our intensive care unit. Several needle holes were found over his forearm and the urine drug screen was positive for morphine. Broad spectrum antibiotic was prescribed for pneumonia and his SBP was around 80-90 mmHg with the use of inotropic agents. His hemodynamic status became stable after treatment and the conscious level improved gradually 6 days later after a period of delirium. He was extubated successfully and was transferred to an ordinary ward. Heroin withdrawal syndrome with symptoms of irritation, insomnia, chills and craving was observed and diagnosed by the psychiatrist. He showed a strong inclination to continue methadone replacement therapy. The pneumonic patch was resolved after treatment and he was discharged following 3 weeks of hospitalization.

However, progressive bradykinesia and decreased verbal output were found after discharge. Then rigidity of all four limbs, incontinence and mutism appeared. He became bed-ridden and totally dependent 3 weeks after discharge (6 weeks after the onset of the insult). He was admitted again 7 weeks after the onset due to low grade fever and possibilities of pneumonia. The neurological

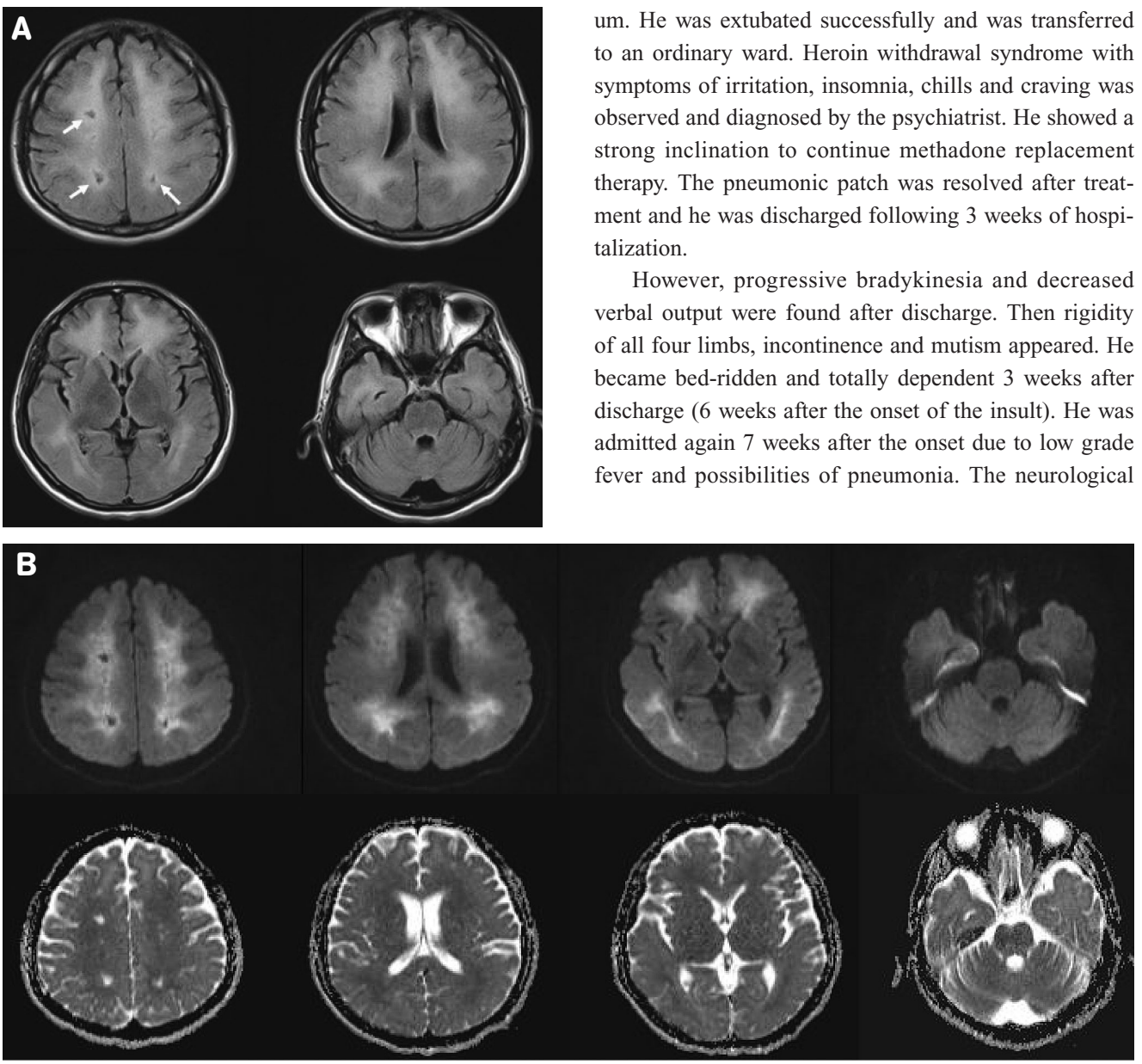

Figure 1. (A) Brain MRI 47 days after the onset of the insult showed diffusely increased signal intensity in the periventricular white matter on FLAIR sequence. Several small vacuolar lesions in bilateral corona radiata were also found (arrow). (B) High signal changes on DWI (upper column) and minimal low signal changes on ADC mapping (lower column) were noted.

examination revealed mutism, sustained leftward gaze, generalized hyperreflexia with bilateral ankle clonus, rigidity and paratonia over four limbs. He could not follow any simple verbal or gestural order. The neurological findings were suggestive of a state of akinetic mutism and left frontal lobe dysfunction. The results of cerebrospinal fluid (CSF) study were unremarkable. Anti-HIV antibody was negative. Magnetic resonance imaging (MRI) of the brain (47 days after the onset) showed diffuse increased signal intensity in the periventricular white matter on fluid-attenuated inversion recovery (FLAIR) sequence (Fig. 1A). High signal on diffusion weighted image (DWI) and minimal low signal change on apparent diffusion coefficient (ADC) mapping were also seen in the same areas (Fig. 1B). The globus pallidus and cerebellum, however, were not involved. Scattered small vacuolar lesions in bilateral corona radiata were also found (arrow). Low dose bromocriptine (7.5 mg per day) was prescribed for the parkinsonian symptoms and akinetic mutism, in the meanwhile we kept supportive care including nasogastric feeding and rehabilitation. During the hospital course, no convulsion was witnessed. The fever subsided gradually and he was discharged after 2 weeks of hospitalization.

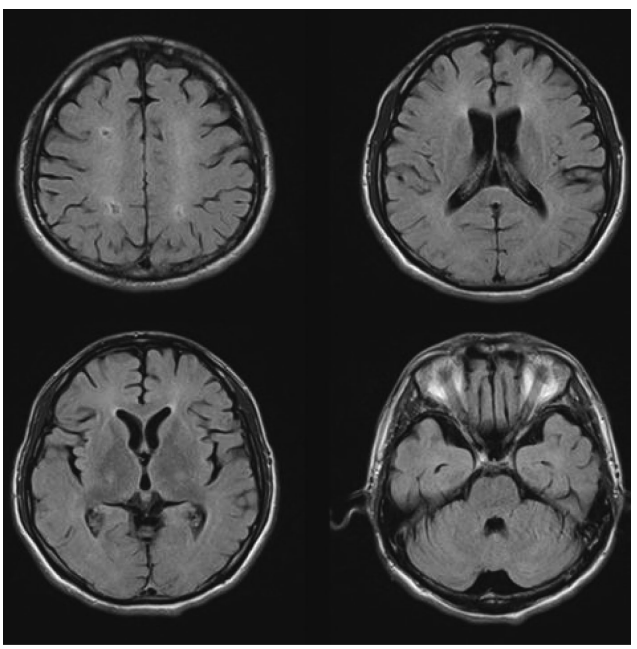

Figure 2. Brain MRI 5 months (day 151) after the onset of the insult showed regression of the white matter lesions but presence of mild cortical atrophy.

After discharge, he was regularly followed up at our neurology clinic. His cognitive function improved gradually and the limb spasticity ameliorated. He was ambulatory 3 months after the onset, but recent memory deficit as well as mild bradykinesia and bradyphrenia persisted. The cognitive abilities screening instrument (CASI) score was 67/100 at that time. The Mini-Mental State Examination (MMSE) scores were 18/30 and 22/30 3 months and 5 months after the onset of the insult, respectively. Retrograde and anterograde amnesia was found and he could not recall any event between 1 month before and 3 months after the onset of the insult. Brain MRI 5 months after the onset showed significant improvement in the white matter hyperintensity, but mild generalized cortical atrophy was found (Fig. 2).

DISCUSSION

Different routes of heroin addiction can cause different complications. Inhalation of heroin vapor ("chasing the dragon") can cause a toxic spongiform leukoencephalopathy[1-2] and intravenous heroin causes hypoxic-ischemic leukoencephalopathy (HIE).

Heroin overdose can cause hypoxia due to respiratory depression and hypotension. The usual pathologic finding of hypoxia in central nervous system (CNS) consists of damage to the neurons of the cerebral cortex and various subcortical gray matter structures (typically at globus pallidus)[3]. Selective injury to the cerebral white matter as a consequence of hypoxia-ischemia is less common. HIE tends to occur when the hypoxemia is prolonged and associated with periods of hypotension and metabolic imbalance[3]. Chalela et al. found that prominent, symmetric restricted water diffusion (confirmed by ADC maps) can occur early after HIE in the white matter[4].

Delayed neurological deterioration after anoxia is uncommon. It can be seen under several circumstances like poisoning, anoxic anoxia, anesthesia and cardiac arrest. Following a lucid interval of days to weeks, progressive neurological deterioration appears. It may lead

to coma and death at any point. In these cases, demyelination in the cerebral hemisphere without significant neuronal damage consistently composes the cardinal pathological abnormality[5]. In carbon monoxide (CO) poisoning, there is usually involvement of the basal ganglia[6]. Heckmann et al. hypothesize that the delayed encephalopathy is caused by the selective necrosis of myelin-producing glia cells in the borderzone areas of the white matter[7]. The clinical consequences would be delayed due to the long half-life of myelin (2.5-8.7 days) as the necrosis of the myelin sheaths is known to follow the cell necrosis after 10-14 days[8]. However, the exact underlying pathogenesis remains unknown. Individuals with relative deficiency of arylsulfatase A were reported to be especially susceptible to delayed hypoxic neuronal injury[9]. The lack of a correlative history and pallidal necrosis makes CO poisoning not likely in this reported case. Symmetric abnormalities involving the cerebellar white matter and posterior limb of the internal capsule are the characteristic neuroimaging features (brain MRI) of heroin vapor inhalation toxicity[2], but were not present in this reported case either.

Only a few cases of delayed leukoencephalopathy after intravenous heroin overdose have been reported[10-12]. Clinically, it resembled delayed neurological deterioration after anoxia but the prognosis varied. Barnett et al. reported a case with good clinical recovery after 9 months of follow-up[11]. The initial brain MRI in that case revealed diffuse bilateral cerebral white matter high signal changes on FLAIR sequences and on T2-weighted imaging. Almost complete resolution of the diffuse white matter signal changes but development of volume loss were found on subsequent MRI. Rizzuto et al. reported another patient who died eventually[12]. The neuropathological study of the brain disclosed pale, spongy myelin with diffuse reactive astrogliosis and microglial proliferation, yet there was no necrotic changes in the globus pallidus typical of hypoxic damage and the definite pathogenesis remains unexplained. Although DWI and ADC mapping were not mentioned in the previous reports. The high signal on DWI and minimal low signal on ADC mapping in this reported case suggest that cytotoxic edema is not the only pathology. Myelin spongiosis and subsequent gradual remyelination during clinical recovery should also be considered. The tissue loss in bilateral corona radiata and mild cortical atrophy suggest some irreversible damages, which may be due to axonal fallout secondary to myelin spongiosis[11]. Although the previous reports of delayed hypoxic leukoencephalopathy have indicated no effective clinical parameter to predict the prognosis and no known treatment, the potential of recovery from CNS myelin injury has been mentioned, and early diagnosis with supportive care advocated[11].

In conclusion, we suppose that hypoxia caused the delayed leukoencephalopathy in this reported case, and heroin injection may augment the injury. Our patient made a significant but incomplete recovery in his cognition and motor function within a relatively short period (3-6 months). Early diagnosis of delayed leukoencephalopathy is emphasized, and timely supportive treatment, complication prevention and rehabilitation are strongly recommended. Such patients may pick up and continue to have more recovery somewhere in the course of the disease .

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