Case Report: The Spastic Weakness of the Lower Extremities Following Methadone Poisoning: A Case Report



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ABSTRACT

Background: Delayed Post-Hypoxic Leukoencephalopathy (DPHL) is a demyelinating syndrome that typically occurs in the form of progressive acute encephalopathy from a few days to weeks after apparent recovery from a coma due to prolonged cerebral hypoxia. In this article, we present a case that developed spastic weakness of the lower extremities 3 months after hypoxic coma. The patient was eventually treated following a diagnosis of DPHL.

Case Report: A 28-year-old patient presented with a history of hypoxic coma following methadone overdose 3 months prior to referral with progressive lower limb weakness. Neurological examination presented weakness of 4.5 lower limbs with hyperreflexia, clonus, and Babinski reflex. Imaging data indicated a broad symmetrical involvement of the logical hemisphere white matter with delayed leukoencephalopathy after hypoxia. Furthermore, all the tests requested for the patient provided data in the healthy range.

Conclusion: DPHL is a unique clinical syndrome that requires high diagnostic suspicion along with additional laboratory and imaging findings. An essential point in the present report is the presentation of the spastic weakness of the lower extremities as a rare manifestation of DPHL.

1. Introduction

ypoxic-ischemic encephalopathy is among the major causes of long-term neurological dysfunction. It is often secondary to carbon monoxide poisoning or overdose of opioid compounds. With

the recent treatment systems advances, more individuals are recovering from hypoxia. However, depending on the severity of the brain injury, different neurological complications may remain in the patient [1]. Delayed Post-Hypoxic Leukoencephalopathy (DPHL) is a rare phenomenon that manifests as progressive encephalopathy with agitation, mutism, and sometimes mania after 1-4 weeks of initial recovery. Sometimes, the syndrome manifests in the form of progressive encephalomyelopathy with extrapyramidal symptoms; it eventually leads to coma and death, although in numerous cases, a relative improvement is detected in symptoms [2, 3].

* Corresponding Author: Seyed Amir Hejazi Address: Neuroscience Research Center, Faculty of Medicine, Qom University of Medical Sciences, Qom, Iran. Phone: +98 (912) 3062043 E-mail: assh.hejazi@gmail.com In this article, we present a patient who, after complete recovery from a hypoxic coma following methadone overdose, developed spastic weakness of the lower extremities. The reported patient was finally treated for DPHL.

2. Case Report

The patient was a 28-year-old man with a complaint of progressive symmetric weakness of the lower limbs since a month before referral. According to the patient, the problem was first wearing the shoes and then going up and down the stairs and getting up from a sitting position. He presented no history of sensory disturbance, sphincter disorder, exacerbated symptoms in heat (uhthoff's sign), electric shock following bending of the head (lhermitte's sign), pain, fatigue, or systemic symptoms in the form of weight loss and night sweats.

He reported a history of drug intoxication with methadone and hypoxic coma 3 months before referral. According to the patient's brief record, he was admitted to the emergency room 3 months before the incident, following methadone overdose with decreased consciousness and irregular breathing. At that time, the patient was in a deep coma with 7.15 Glasgow Coma Scale (GCS). Systemic examinations suggested a blood pressure of 80.60 mm Hg, a pulse rate of 50, a respiratory rate of 8, and a temperature of 36.5 °C. On neurological examination, the pupils were mitotic and non-reactive to light. Corneal and vestibulovascular reflexes were healthy. The plantar patient was immediately intubated and given naloxone, which led to a relative recovery. He was then hospitalized in the intensive care unit for 20 days and underwent supportive treatment. Remarkably, the brain serial imaging of the patient was normal at that time. Twenty days later, the patient was discharged in good general conditions with a normal neurological examination.

At the second time of referral to neurology clinic: The patient was alert and oriented to the time, place, and person. The examinations of memory, speech, and cranial nerves were normal. There was no evidence of atrophy, fasciculation, or muscle tenderness on motor examination. The force of the neck muscles and upper limbs was normal. The muscle power of lower limbs was 4/5 with hyperreflexia and clonus. Babinski's reflex was also positive on both sides. Sensory examinations were normal and no sensory level was obtained. The study patient's gait was spastic.

The patient underwent complete biochemistry and blood cell tests; accordingly, the results of which were normal. The brain Computed Tomography (CT) revealed an extensive hypodense lesion in bilateral hemispheric white matter. Supplementary the brain Magnetic Resonance Imaging (MRI) revealed symmetrical signal change in the white matter of bilateral hemisphere without involvment of the cerebellum, brain stem, and the gray matter. The lesion was not stained after contrast agent injection (Figure 1). The cervical and thoracic MRI was unremarkable. Complete vascular collagen tests were requested, all of which were normal. Subsequently, the patient underwent lumbar puncture. The where analysis, IgG index level, and cerebrospinal fluid culture were normal and no oligoclonal band was found in cerebrospinal fluid. Besides, no abnormal findings were found in the visual evoked potential test.

The patient received intravenous methylprednisolone pulse (1000 mg daily in one liter of 5% dextrose serum) for 5 days without any alternations neurological status. After seven days of hosptalization, the patient discharged home with simialr examination to the time of arrival.

At the patient's quarterly follow-up for one year, The patient gradullay revealed clincial improvement. At the end of one year, the lower extremity force was normal and only hyperreflexia was evident in the lower extremities. Moreover, the brain MRI findings revealed a reduction in voulme of lesions.

3. Discussion

In the presented patient, MRI findings suggested extensive hemispheric white matter damage without gray matter involvement. Additionally, the brainstem and cerebellum were significantly normal; thus, these data were in favor of DPHL. The diagnosis of DPHL was based on the rule out of other causes of encephalopathy and the presence of of supportive findings, such as extensive demineralization of white matter hemispheres without the involvement of brainstem and cerebellum, and increased myelin base protein levels in cerebrospinal fluid [3, 4]. In our patient, all evaluated tests were negative and due to the history of prolonged hypoxia induced by opioid poisoning, the patient's myelopathy was attributed to DPHL.

Leukoencephalopathy associated with opioid compounds has been discovered since the 1970s. The most significant clinical syndromes include chronic encephalopathy following long-term use of opioid compounds and, less commonly, delayed hypoxic leukoencephalopathy. In this case, patients seeking almost complete recovery from a coma due to opioid poisoning, suddenly develop various symptoms. Progression and death due to extrapyramidal symptoms, corticospinal symptoms, and behavioral changes might occur. However, most of the symptoms improve within a few weeks [5].

The exact pathophysiology of this disease remains unclear. The prolonged hypoxia of subcortical white matter due to impaired oxygen delivery or hypotension appears to disrupt ATP-dependent enzymatic pathways; such processes lead to myelin circulation and subsequently delayed demyelination [6]. In the study by Sputcher et al., the evidence of demyelination with increased myelin-based protein in the cerebrospinal fluid in a case of DPHL associated with prolonged coma following opioid poisoning supported the role of myelin-based protein in this disorder [4]. There are also reports of arylsulfatase deficiency in patients with DPHL [7]. In another study, an autopsy of a patient with DPHL revealed evidence of subcortical myelin sheath loss without U-fiber involvement with prominent macrophage/microglial inflammation and extensive axonal damage [8]. Animal models have also signified that delayed neuropathology induced by carbon monoxide poisoning depends on the inflammatory cascade reaction of myelin-based protein and malonyl aldehyde. Thus, following the structural modification of basal myelin protein due to exposure to carbon monoxide, inflammatory cells, such as macrophages and T lymphocytes enter the brain cells of mice; accordingly, an auto-proliferative reaction occurs in the excess of myelin-based protein [9].

The main reports of DPHL are in the form of sudden behavioral disorder after a period of recovery following hypoxic coma. In a study, Spercher et al. [4] examined 3 patients who developed mental health disorders after several weeks of hypoxic coma. The first patient was a 39-year-old woman who developed encephalopathy and hyperreflexia 4 weeks after coma due to opioid and cocaine poisoning. Moreover, there was evidence of increased levels of myelin-based protein in the cerebrospinal fluid and elevated acetyl aspartate on spectroscopy. At a one-year follow-up, the patient manifested relative improvement in symptoms with some degrees of attention deficit and reduced demyelinating lesions. The second explored patient was a 51-year-old woman who completely recovered from coma after methadone use; subsequently, the patient presented symptoms of hypokinetic - rigid mutism with increased levels of myelinbased protein in the cerebrospinal fluid after 21 days. Remarkably, the patient recovered after 38 weeks. The third patient was a 56-year-old woman who experienced coma and rhabdomyolysis following fentanyl, opioid, and benzodiazepine poisoning. The patient developed progressive hypokinetic encephalomyelitis 15 days after discharge, which failed to improve after two months [4].

In another study, two patients with encephalopathy associated drug-induced hypoxic coma and non-specific diffuse changes in the hemispheric white matter and elevated myelin-based protein levels were treated for



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Figur 1. Evidence of bilateral hypersignal changes in hemispherical white matter symmetrically without U-fiber involvement in the T2 sequence

DPHL. To the best of our knowledge, there is no report of isolated spastic paraparesis as a manifestion of DPHL. in our case, according to the clinical scenario, laboratory findings, and imaging data, there was no justifiable cause. Finally, significant clinical improvement and reduction of lesions in one-year follow-up supported the diagnosis of DPHL.

4. Conclusion

DPHL is a unique clinical syndrome that requires high diagnostic suspicion along with confirmatory laboratory and imaging findings. Most patients develop a sudden behavioral disorder after a few weeks of initial symptoms recovery. however, most patients gradually improve. An essential point in the present report was the presentation of the isolated spastic weakness of isolated spastic paraparesis as a rare manifestation of DPHL.

Ethical Considerations

Compliance with ethical guidelines

There were no ethical considerations to be considered in this research.

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Authors' contributions

All authors equally contributed to preparing this article.

Conflict of interest

The authors declared no conflict of interest.

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