H119 Delayed Post-Hypoxic Leukoencephalopathy (DPHL)

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After attending this presentation, attendees will understand how to conduct the unusual diagnosis, DPHL, and appreciate its causes, differential diagnosis, and neuropathological substrates.

This presentation will impact the forensic science community by enlightening attendees regarding DPHL and by highlighting the unnatural causes of the syndrome.

A 20-month-old infant was taken to a hospital for fever and diarrhea. While being held down on his back, for a rapid Strep swab, he vomited, aspirated, and developed respiratory distress with hypoxia. A chest X-ray revealed dense consolidation in the right upper and middle lobes of the lung. He was intubated and began to require medication to maintain blood pressure. The infant's condition worsened and he developed acute respiratory distress syndrome and cardiac failure. The cardiac function recovered after a few days of extracorporeal membrane oxygenation. Despite the stabilization of his cardiopulmonary status, he had suffered severe cerebral hypo-oxygenation. Following hospital discharge, the infant had a dense left hemiparesis, but had use of his right arm and was improving with therapy. He was beginning to feed himself and was smiling and using several words. Three months later, his neurologic status deteriorated. The Magnetic Resonance Imaging (MRI) of the brain revealed diffusely abnormal white matter. The differential diagnosis included storage diseases, cerebral infections, vanishing white matter disease, and delayed post-hypoxic leukoencephalopathy. Years later, at 5 years of age, his mother fed him through his gastric feeding tube and put him in bed to nap. She later found him unresponsive and not breathing. An autopsy revealed a diagnosis of DPHL.

DPHL is a rare and under-recognized demyelinating syndrome. To date, autopsy and histologic descriptions of this entity are rare. This presentation reports an autopsied case of DPHL and discusses the histologic findings and differential diagnosis.

In the typical, two-stage presentation of DPHL, there is a recovery from a comatose state, followed later by an acute onset of neurologic signs and symptoms. There are no formal criteria for the diagnosis of DPHL, though clinical history and white matter changes are sufficient if other etiologies have been excluded.

DPHL is considered a distinct process in contrast to other direct causes of acute leukoencephalopathy. DPHL was originally described as sequelae of carbon monoxide poisoning and has recently been associated with the use of drugs of abuse. Though its pathophysiology is not understood, carbon monoxide, heroin, and benzodiazepine may be directly myelinotoxic. DPHL from drug exposures is similar to that from other forms of hypoxia; therefore, it is unclear whether neurotoxicity from heroin or other impurities in addition to hypoxia alone is involved. A period of prolonged cerebral anoxia is a common feature of all cases of DPHL. DPHL has also been described in a setting of strangulation and hemorrhagic shock; therefore, cerebral hypo-oxygenation is sufficient to cause DPHL without a specific toxic mechanism.

The gross neuropathological findings include profound widespread degeneration of the white matter with relative sparing of the u-fibers, the gray matter, and the cortical ribbon. The white matter demyelination is associated with the presence of macrophages and reactive astrocytes. It has been proposed that it is damage to glial cells in the

white matter that is responsible for the demyelination. It has also been suggested that arylsulfatase A deficiency predisposes susceptible individuals to DPHL and lactic acidosis is the pathogenesis of this disorder. In this case, there was extensive myelin loss in white matter in a severely vacuolated background neuropil and immunohistochemical staining confirmed the diagnosis. The cause of the demyelinating syndrome in this case was pure hypoxia without the presence of drugs of abuse.

Neuropathology, Leukoencephalopathy, Cerebral Hypoxia