H1 A Rare Presentation of Alexander Disease

Edana D. Stroberg, DO, Office of the Chief Medical Examiner, 901 N Stonewall Avenue, Oklahoma City, OK 73117; Kenneth D. Hutchins, MD, Miami-Dade County, Medical Examiner Department, Number One on Bob Hope Road, Miami, FL 33136; and E.O. Lew, MD, Miami-Dade County, Medical Examiner Department, Number One on Bob Hope Road, Miami, FL 33136-1133*

After attending this presentation, attendees will better understand Alexander disease, a rare leukodystrophy, and its presentation.

This presentation will impact the forensic science community by increasing attendees' understanding of Alexander disease and the importance of a thorough neuropathologic evaluation in cases of anoxic encephalopathy.

Introduction: Alexander disease is an extremely rare, usually progressive and fatal, neurological disorder.[1] Initially, it was detected most often during infancy or early childhood, but as better diagnostic tools have become available, it has been found to occur with similar frequency at all stages of life.[1] Approximately 95% of Alexander disease cases are caused by mutations in a gene named *GFAP* for a structural protein called glial fibrillary acidic protein that is found exclusively in astrocytes in the central nervous system.[1] Alexander disease has been estimated to occur at a frequency of approximately one in one million births.[1] There are three forms of Alexander disease: infantile, juvenile, and adult. Juvenile Alexander disease is characterized by difficulty in talking and swallowing and the inability to cough.[2] There can also be weakness and spasticity of the extremities, particularly the legs.[2] Unlike the infantile form of the disease, mental ability and head size may be normal.[2] Survival can extend several years following the onset of symptoms, with occasional longer survival into middle age.[2] The course of the disease may involve signs of swallowing or speech difficulty, vomiting, ataxia, and/or spasticity and kyphoscoliosis can occur.[2] The most striking neuropathological feature is the diffuse presence of eosinophilic fibrinoid bodies in the cytoplasm of fibrillary astrocytes.

Material and Methods: The decedent was a 14-year-old girl with a history of narcolepsy, sleep apnea, and scoliosis. Eighteen months prior to her death, the decedent and several others were playing in a backyard pool. When the decedent did not resurface, one of the children notified the supervising adult, who pulled her out of the pool. She was transported to a local hospital and recovered; however, she began to display signs of global developmental delay with onset of impulse control issues, anxiety, depression, self-mutilating behaviors, dysphagia with bouts of aspiration pneumonia, and ataxia. Two weeks prior to her death, she was hospitalized for self-mutilation and her condition progressed to her refusing to eat, talk, or get out of bed. She was also found to be bradycardic and hypothermic. She became unresponsive and was found to have worsening cerebral edema with cerebellar tonsillar herniation.

Results: At autopsy, she was found to have cerebral edema and scoliosis of the thoracic spine. Neuropathologic consultation revealed a non-perfused, respirator-type, macerated brain and spinal cord with diffuse collections of eosinophilic fibrinoid bodies (Rosenthal fibers) in all sections.

Conclusion: The decedent experienced a near-drowning episode and was diagnosed with anoxic encephalopathy when she was 12 years old. Afterward, she experienced a myriad of psychiatric and neurologic issues that were determined to be sequelae of anoxic encephalopathy. A Magnetic Resonance Imaging (MRI) of her brain revealed atrophy of the cervical spinal cord and periventricular white matter changes, which can be seen in both Alexander disease and anoxic encephalopathy. She became unresponsive in the hospital and care was withdrawn after the girl had been on a respirator for multiple days. At autopsy, she had a non-perfused, macerated brain and spinal cord, which is a known complication of being on a respirator. Her brain and spinal cord were submitted for neuropathologic evaluation, which revealed Alexander disease. The decedent experienced onset of the disease at approximately 12 years of age, which unfortunately coincided with a near-drowning event with resultant anoxic encephalopathy, thus confounding her clinical course. This case highlights the importance of performing a thorough neuropathologic evaluation when necessary, even when it is presumed to be of little informative value because of autolytic changes in the brain.

Reference(s):

1. Goldman, James E. Alexander Disease. *NORD (National Organization for Rare Disorders)*. n.d. Web. 14, June 2017.
2. Alexander Disease. *United Leukodystrophy Foundation*. n.d. Web. 14 June 2017.

Alexander, Leukodystrophy, Anoxic

*Presenting Author