CASE 9

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Clinical Abstract:

The patient was a 22 month old girl who was born at term by spontaneous vaginal delivery after an uneventful pregnancy. She was given hepatitis B prophylaxis shortly after birth because her mother is a known carrier. She developed normally until the age of six months when developmental and growth arrest were noted. She had wandering eye movements and ptosis. By 12 months, she was below the fifth percentile in height, weight, and head circumference. A sweat test was negative and thyroid function tests were normal. At 16 months, she had lost previously acquired milestones, was less active, and interacted less with others. Audiometry testing indicated moderate bilateral hearing loss. At 19 months, a karyotype was performed and interpreted as 46,XX. A serum amino acid screen showed an increased alanine level. Evaluation at Children's Hospital included blood levels of arylsulfatase, galactocerebrosidase, galactosidase, long chain fatty acids, and phytanic acid; all results added no further diagnostic information. A T_1 and T_2 weighted MRI at 21 months showed increased signal of the thalamus (bilateral), pons and midbrain with decreased differentiation between grey and white matter. Two weeks after the MRI, she was admitted to MCHV for further studies. Physical examination revealed a lethargic child with symmetrically decreased muscle tone throughout. Elevated serum levels of pyruvate, lactate, and alanine, and elevated CSF levels of pyruvate and lactate, were noted. Serum ammonia was normal. EMG and nerve conduction velocities were unremarkable. She was discharged after a few days, but was readmitted following two weeks of decreased tone and decreased responsiveness to verbal and tactile stimuli. On the day before admission, she developed fever, loose black stools, and vomiting. On the morning of admission, her parents found her lying in vomitus, unresponsive, and with cold, blue extremities. She was brought to the Emergency Department where she was noted to be cyanotic with gasping respirations and hypotension. Resuscitation efforts included intubation and pressor support, but she developed decerebrate posturing with loss of pupillary and corneal reflexes. Although pupillary reflexes returned within 24 hours, respirator support was withdrawn in consideration of her generally poor prognosis. She died 2 days following admission.

Autopsy Findings:

The major autopsy findings were growth retardation, bronchopneumonia, and left ventricular hypertrophy. The brain weighed 965 grams. In the thalamus bilaterally were focal discolorations measuring 1 to 4 mm, primarily in the ventral aspects. Similar lesions were noted in the pons and midbrain.

Material Submitted: One H & E slide of an autopsy brain section.

Points for discussion: 1. Diagnosis

2. Pathogenesis