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Prof. Dr. K. WIDHALM
University of Vienna, Department of Pediatrics
Währinger Gürtel 18-20, A-1090 Vienna

ABSTRACT FORM

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SUCCESSFUL DCA TREATMENT IN A PATIENT WITH LEIGH DISEASE

Duangrurdee Wattanasirichaigoon, Fran Dougherty
Children's Hospital, Harvard Medical School, Boston, MA02115

Leigh disease is a rapidly progressive, fatal demyelinating disease of the brain. Most cases are found to result from defects in mitochondrial electron transport chain energy production or pyruvate metabolism. Although effective treatment is unavailable, DCA (dichloroacetate) trials in several cases have shown questionable benefit. By stimulating the PDH complex, DCA shunts pyruvate away from lactate production. We report a 22 month-old girl with Leigh disease, who showed marked improvement following initiation of DCA therapy. The patient presented to us at 1 year of age with failure to thrive, severe developmental delay (functioning at 2-3 months of age), extremity tremor and truncal ataxia, hypotonia, ophthalmoplegia, vertical and horizontal nystagmus, and poor head control. Pertinent lab findings included chronically elevated blood lactate level to 6.4 mmol/l, metabolic acidosis (pH 7.27 from both lactate and RTA type II), and MRI changes (increased T2 signals involving the medulla, dorsal pons, entire midbrain, cerebral peduncles and medial thalami, as well as the periventricular white matter. A 50 mg/kg/day DCA was initiated with normalization of her blood lactate within three days. Supplemental bicarbonate therapy was also added for treatment of RTA. Six weeks after beginning DCA therapy, she was noted to exhibit age-appropriate cognitive, language, and attentional skills whereas her gross and fine motor skills were delayed at 10 month level. Her ophthalmoplegia, tremor and ataxia almost completely resolved. A repeat MRI 8 months after DCA initiation revealed a decrease of abnormal T2 signals at the thalami and brain stem region. She has continued growing and making slow but steady developmental progress. Subsequent biochemical (PDH complex assays in skin fibroblast and muscle, pyruvate carboxylase activity in skin fibroblast, and electron transport chain muscle assays) and molecular (mt DNA analysis for the common MELAS, MERRF and NARP mutations) studies have failed to identify her underlying defect. We believe she is the first Leigh disease patient to show marked clinical, neurodevelopmental, neuroimaging and biochemical improvement following DCA therapy.

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AUTHOR'S CORRESPONDENCE ADDRESS:

LAST NAME WATTANASIRICHAIGOON FIRST NAME DUANGRURDEE TITLE M.D. SEX M F
ADDRESS 300 Longwood Ave - Children's Hospital
POSTAL/ZIP CODE 02115 CITY Boston COUNTRY U.S.A
TELEPHONE (617) 355-7572 FAX (617) 355-7588

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