L-Carnitine as a Treatment for Rett Syndrome

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ABSTRACT: A 17-year-old girl with Rett syndrome, who was taking no other medications, was treated with L-carnitine (50 mg/kg/day). Within 2 months of initiation of treatment, she became much more alert, developed good eye contact, started reaching for objects with both hands, and answered simple questions with one or two words. L-carnitine was discontinued and within 1 week she lapsed into her pretreatment condition of lethargy with no interest in her environment, not reaching for objects, poor eye contact, and not speaking. One week after L-carnitine was resumed, she again became alert, started reaching for objects, and saying one or two words. Her serum carnitine levels (free and total) were within normal limits before and after L-carnitine treatment, but were higher while she was taking L-carnitine. Her serum ammonia was within normal limits prior to starting L-carnitine. L-carnitine appears to be an effective treatment for this girl with advanced Rett syndrome.

RETT SYNDROME is a progressive neurologic disorder in girls first described by Rett in 1966.[1] There is no known effective treatment of this condition. Mitochondrial abnormalities have been described in Rett syndrome, including swollen and dumb-bell shaped mitochondria in muscle biopsy specimens[2,3] and large, swollen mitochondria with scant cristae in nerve biopsy specimens.[4] Carnitine has two principle functions: to transport long-chain fatty acids into the mitochondrion and to help regulate the intramitochondrial ratio of acyl-coenzyme A (CoA) to free CoA.[5] Mitochondrial carnitine deficiency impairs energy metabolism by restricting mitochondrial beta-oxidation of long-chain fatty acids and by permitting build up of acyl-CoA within the mitochondrion resulting in dysfunction in those tissues most dependent on mitochondrial energy metabolism: brain and muscle.[5] Because Rett syndrome has been associated with mitochondrial structural abnormalities that may indicate functional mitochondrial abnormalities and because L-carnitine is an effective treatment for selected cases of mitochondrial carnitine deficiency, we treated one Rett syndrome patient with L-carnitine.

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CASE REPORT

The pregnancy was without complications. The patient was born to a 21-year-old gravida 2, para 1 mother after a full-term pregnancy. Labor started spontaneously and she was born of a vaginal, vertex presentation with a birth weight of 7 lb and 11 oz. Her 1 minute Apgar score was 10. At birth her head circumference was 33 cm (50th percentile). There were no postnatal difficulties. The possibility of developmental delay was raised at 6 months of age, but she was able to walk independently at 14 months of age.

At 5 years of age she failed preschool and on informal testing was noted to have expressive and receptive language delay, poor visual skills, and an overall cognitive level of a 3-year-old. At 6 years of age her Stanford Binet IQ was 39. Between 6 and 7 years of age, her gait started to deteriorate and she became progressively more ataxic. At this time she also started to lose verbal abilities. At 8 years of age her head circumference was 48 cm (below the 2nd percentile) and she had a developmental age of 32 months. At 12 years of age she was admitted to Marklund Children's Home. At that time she was able to walk with assistance and speak in one- and two-word sentences. Over the following 2 years she lost all walking and speaking abilities. At 13 years of age, she required a gastrostomy tube due to progressive dysphagia. The tube has been used since then to provide supplemental feedings. When she was 15 years of age, her Slosson scale revealed a mental age of 1 year and 3 months and social-emotional development of 3 months. Her head circumference was 49 cm (4 standard deviations below the mean). When she was 17 years old, her head circumference remained 49 cm. Her weight was 33.3 kg (4 standard deviations below the mean) and height was 148 cm (below the 2nd percentile). On examination she had no dysmorphic features, organomegaly, or any signs of a neurocutaneous disorder. Neurologically she was nonverbal, did not respond to any verbal commands, and had hypertonia and hyperreflexia.

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