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"Carnitine Supplementation for the Management of Autism Spectrum Disorder Associated with TMLHE Gene Deletion"

Abstract

Autism spectrum disorder (ASD) involves multiple, varying presentations which often includes early onset challenges in speech, learning, behavior, and social cues. ASD is estimated to occur in 1 % of the population. It has been reported that deletion of portions of the trimethyllysine hydroxylase epsilon (TMLHE) gene, found on the X chromosome, is an inborn risk factor for ASD. Trimethyllysine hydroxylase, encoded by TMLHE, is the first enzyme in the biosynthesis of carnitine, a transporter for long fatty acids into the mitochondrion. Abnormal fatty acid metabolism in the central nervous system has been associated with autism. In addition, it has been shown that patients with the TMLHE gene mutation respond favorably to carnitine supplementation, as the 4-year-old patient ceased regression and even began to reach more milestones in his development.

Patient is a 14-year-old male diagnosed with autism spectrum disorder (ASD) who was referred to Dr. Regina Zambrano for genetic testing. The chromosomal microarray results arrived on the 24th of March 2023, and showed a deletion of the terminal site: Xq28. Genetic testing was also performed on the patient's mother and showed that one of her X chromosomes also possessed this Xq28 deletion. The patient tested negative for Fragile X syndrome, a common cause of ASD. Because the TMHLE gene is found in Xq28, and encodes a necessary step of carnitine synthesis, the patient was tested for his carnitine levels. His total carnitine concentration in plasma was 24 mcmol/L (<30 mcmol/L is considered low), and his free carnitine was 18 mcmol/L (<20 mcmol/L is considered low). As demonstrated by Ziat et al., a patient with a mutation in TMLHE responded favorably in the management of their autism with carnitine supplementation. Based on this previous case, this patient has been prescribed a carnitine supplement. The patient's current weight is 120 lb (54.4 kg). The patient will take carnitine supplements two times per day.

The only medication the patient currently takes is oxcarbazepine for previous incidents of seizures. Currently, no link is found between oxcarbazepine and carnitine deficiency, though other anti-epilepsy treatments such as valproate are a risk factor for developing secondary carnitine deficiency.

The patient is currently monitored for improvement in his ASD, including speech improvements (patient is currently nonverbal), social awareness, grades in school, and changes in behavior.