A case of Very long-chain acyl-CoA dehydrogenase deficiency with new mutation and favorable response to L-carnitine, Riboflavin, and CoQ10

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Very long-chain acyl-CoA dehydrogenase (VLCAD) deficiency is a condition preventing the body from transforming certain fats to energy, principally during periods without food (fasting). Signs and symptoms of VLCAD deficiency classically manifest during infancy or early childhood with hypoglycemia, lethargy, muscle weakness, and episodes of dark urine. There is no approved treatment for such patients.

A 38-year-old man was referred for a very slowly progressive lower limb weakness since childhood with the inability to climb upstairs since two years before. He reported episodes of dark urine after exercise. He had no history of provokative afctors such as trauma, administration of drugs, infections and other factors triggering rhabdomyolysis. There was no similar case in the family. On examination, he had a weakness of neck flexion, bilateral arms abduction (MRC grade 3), bilateral elbow flexion (MRC grade 4), bilateral hip flexion (MRC grade 4), and bilateral knee extension (MRC grade 4) with normal deep tendon reflexes. The functional scale of Brooke for upper extremities was three (out of 6) and the functional scale of Vignos for lower extremities was four (out of 10).

The CK was 5400 IU/L; cardiac exams were normal; and electromyography was myopathic in proximal muscles of upper and lower limbs. Muscle MRI revealed moderate fat deposition in paraspinal muscles, adductor and vastus muscles as well as medial heads of gastrocnemius muscles. On muscle biopsy, myopathic atrophy of mainly type I fibers with multiple necrotic/regenerative fibers and fine lipid droplets in muscle fibers in ORO stain was seen. Targeted next-generation sequencing for metabolic

myopathies revealed a pathogenic variant defined as c.900G>A (p.Met300Ile) in exon 10 of ACADVL gene due to VLCAD deficiency (MIM#201475).

Segregation analysis for the parents confirmed the heterozygote status of both father and mother (carrier status) for ACADVL gene. We started L-carnitine 2 grams daily, CoQ10 300 mg daily and riboflavin 300 mg daily with a favorable response, and after one month the patient was able to climb upstairs without aid. The functional scales of Brooke and Vignos were both one.

Discussion

Hamano et al reported a 30-year-old man with VLCAD deficiency presenting recurrent rhabdomyolysis. Since the age of 18-year-old with recurrent episodes of exercise induced limb muscle pain, limb weakness and dark colored urine. Several reports showed that muscular form (adult onset form) of VLCAD deficiency demonstrated recurrent rhabdomyolysis, but true 'adult-onset' case with VLCAD deficiency have been rarely reported (Hamano et al. 2003).

It is significant that in the majority of reported VLCAD deficiency patients, there exist episodic symptoms of dark urine and weakness after exercise; however, in our patient the muscular weakness reached a persistent status with a fixed weakness and visible muscle MRI changes.

In patients with muscular symptoms such muscle aching a regimen with a medium-chain fat-rich meal directly before exercise, may be beneficial; however, in asymptomatic mild cases, a fat-reduced diet may not be required, although in later infancy and adolescence, vigorous physical activities may necessitate supplementary energy from medium-chain fat (Spiekerkoetter 2007).

In sum, it seems that a cocktail of L-carnitine, CoQ10, and riboflavin may be an optimal option for this very rare form of lipid storage myopathy.