Diagnosis and Long-Term Treatment of Arginase 1 Deficiency
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Introduction

Arginase 1 Deficiency (ARG1-D), is a rare inborn error of metabolism caused by mutations in the ARG1 gene that compromise arginase enzyme activity, leading to persistent high arginine levels that drive development and progression of neurocognitive and neuromuscular manifestations.1,3

- Onset of clinical manifestations typically becomes evident in the first years of life, rather than the first days or weeks as is typical of other area cycle disorders.1,5
- Progressive spasticity, particularly affecting the lower extremities, is a hallmark of ARG1-D. Developmental delay, including missed milestones, as well as short stature, loss of milestone attainment, and intellectual disability are also common.1,6
- Timely diagnosis and initiation of treatment to reduce arginine is essential to improving patient outcomes
- The current standard of care for ARG1-D relies on dietary protein restriction with essential amino acid supplementation to minimize arginine intake while maintaining nutritional status. Many patients also receive nitrogen scavengers to reduce risk of hospitalization owing to hyperammonemia.8
- Available management strategies for ARG1-D rarely achieve recommended plasma arginine levels, and patients continue to experience significant morbidity. Nonetheless, even when suboptimal, reduction of arginine and cumulative arginine toxicity is important for delaying or diminishing progression of manifestations and may promote clinical stabilization.9

This case describes a Hispanic female who was diagnosed with ARG1-D at 11 years of age after referral to genetics and who has since been followed for nearly 15 years.

Medical History (Birth to Genetics Referral)

- The patient’s medical history and clinical profile upon presentation led to initial suspicion of cerebral palsy. Observation of small stature led to referral to endocrinology, and after comprehensive biochemical testing the patient was referred to genetics.

  Figure 1

  - The patient was born in Ecuador and not identified by newborn screening, likely because of limited access or program implementation
  - Delayed speech was observed at 12–13 months of age. By age 5 years, decreased growth and multiple indicators of neuromuscular impairment were evident
  - Suspicion of a metabolic disorder and subsequent genetics referral occurred after basic labs and amino acid testing revealed abnormalities consistent with a urea cycle disorder

Figure 1. Medical History and Observations Leading to Genetics Referral

AA: amino acid; NBS: newborn screening.