Introduction

- Arginase 1 Deficiency (ARG1-D) is a rare, inherited urea cycle disorder (UCD) with progressive, debilitating manifestations driven by persistent high arginine levels.4
  - Some inborn errors of metabolism, including ARG1-D and other UCDs, present with neurologic/neuromotor disorders and may be treatable.5
- Manifestations of ARG1-D typically become evident early in childhood and progress over time.2,6
  - Spasticity, particularly affecting the lower limbs, is a distinguishing feature of ARG1-D compared with other UCDs; additional common clinical manifestations include developmental delay, intellectual disability, seizures, and short stature.6,7
  - Episodes of hyperammonemia are common in most UCDs but are comparatively less frequent and less severe in ARG1-D; however, hyperammonemia does occur in ARG1-D and can be triggered by stressors such as infections.4,8
- Clinical manifestations common to ARG1-D and cerebral palsy (CP) include, but are not limited to, failure to thrive, delayed/missed milestones, seizures, and spasticity, which can complicate diagnosis.8
- There are no therapies approved specifically for ARG1-D. The current standard of care (SOC) relies on dietary protein restriction with essential amino acid supplementation and use of nitrogen scavengers.6
  - The normal plasma arginine range, based on analysis of the large Framingham Cohort, is 40–115 μmol/L; the guideline-recommended level for patients with ARG1-D is ≤200 μmol/L.4
  - Current SOC does not adequately reduce plasma arginine levels, and long-term outcomes are poor.4 Nonetheless, timely implementation of SOC is important to reduce arginine toxicity and risk of hyperammonemia.

Objective

- To describe the medical history, presentation, diagnosis, and management of a patient with CP and subsequently diagnosed with concurrent ARG1-D.

Case Study

Medical History

- The patient is a 5-year-old female born in Honduras and living in Texas with a history of meningitis that led to numerous debilitating symptoms and a subsequent diagnosis of CP.
  - Generalized stiffness and posturing were evident from the time of the meningitis insult.
  - Seizures typically last 3–5 minutes and involve stiffening of upper and lower extremities with a postictal phase lasting 5–6 minutes.
- At 4 years of age, the patient’s antiepileptic medication was changed from phenobarbital to levetiracetam. Levetiracetam was poorly tolerated, and the dose was subsequently reduced.