Infancy (2–5 years) 1–5
Childhood (5–10 years) 1–5
82 (136–309)

• ARG1-D, arginine 1 deficiency; HSP, hereditary spastic paraplegia.

Normal arginine, ammonia, and urea
✔ ✘

• May present with
  - Inability/g415te, nausea/vomi/g415ng , feeding difficul/g415es, poor growth and development, cerebral palsy, decreased motor function

Other manifestations include
  - Variable decline in neuromotor function
  - Variable decline in growth
  - Progressive spas/g415city
  - Loss of sphincter control
  - Loss of functional movement
  - Loss of speech
  - Loss of hearing
  - Loss of vision

In biochemical evaluations
  - Only mild elevation of ammonia (54 µmol/L) was observed
  - No clinical symptoms

Diagnosis of ARG1-D
  - At age 27, the patient accompanied her sister to a visit with a genetic provider and was subsequently diagnosed with ARG1-D during a metabolic genetics clinic visit based on biochemical data, family history, and homzygous loss-of-function mutations (rs1064794165) in the ARG1 gene
  - Following diagnosis of ARG1-D, the patient was placed on a regime of severe protein restriction and treatment with an arginine scavenger (sodium phenylbutyrate and lactulose) was initiated. At a subsequent neurology follow-up, the patient had continued to decline with progression of lower-extremity spasticity, and underwent additional evaluation for potential causes of these symptoms. At this time, treatment with the nitrogen scavenger and lactulose was stopped owing to lack of clinical benefit
  - Despite the patient’s family history, HSP was the suspected diagnosis for >2 years, with no discussion of a disorder of arginine metabolism as the primary diagnosis in the patient’s medical record

Conclusions

• Previous reports have described misdiagnosis of ARG1-D with spastic diplegia as HSP, largely owing to similarities in neurological presentation.
  - Consistent with the literature, the patient described in this case report was misdiagnosed for multiple years despite her family history of ARG1-D, allowing establishment and progression of typical manifestations of the disorder
  - Because ARG1-D (unlike HSP) is a treatable cause of spastic paraplegia, there is a continued need for increased awareness of the disease among healthcare providers and improved recognition of when biochemical and/or genetic testing should be performed